IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON DIVISION

IN RE: ETHICON, INC. PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LIGITATION	**Master File No. 2:12-MD-02327** **MDL No. 2327** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**
THIS DOCUMENT RELATES TO: **ALL PLAINTIFFS LISTED IN PLAINTIFFS' NOTICE OF ADOPTION**	

REPLY MEMORANDUM IN SUPPORT OF PLAINTIFFS' MOTION TO EXCLUDE THE OPINIONS AND TESTIMONY OF DR. DOUGLAS GRIER, M.D.

Plaintiffs submit the following reply to Ethicon's Memorandum in Opposition to Plaintiffs' Motion to Exclude the Opinion Testimony of Douglas Grier, M.D. For the following reasons, Ethicon's opposition should be denied and the opinions offered by Dr. Grier should be excluded in their entirety as set forth in whole in Plaintiffs' Memorandum to Exclude the Opinions and Testimony of Douglas Grier, M.D.

ARGUMENT

I. Dr. Grier should be precluded from testifying about the safety and efficacy of the TVT and Prolift Product designs.

Plaintiffs moved to exclude the design opinions of Dr. Grier in their Wave 1 Memorandum.[1] In ruling on the Wave 1 Motion regarding Dr. Grier, this Court interpreted the term "design" to refer to "opinions about the process of designing a product. Opinions of this sort include, for example, opinions about pre-market product testing and product development."[2]

[1] *See* Ex. A, Plaintiffs' Wave 1 Memorandum in Support of Their Motion to Exclude Certain Opinions and Testimony of Douglas Grier, M.D.
[2] Mem. Op. and Order (*Daubert* Motion re: Douglas Grier, M.D.), No. 2:12-md-02327, at 6-7 (S.D. W. Va. Aug. 31, 2016) [ECF # 2703].

Upon review, the Court found that Dr. Grier had not expressed any opinions specifically regarding designing a product, and therefore Plaintiffs' Motion was denied as moot.[3]

Plaintiffs' challenge to Dr. Grier's design testimony does not specifically focus on the actual process of designing a product. Rather, Plaintiffs specifically challenge Dr. Grier's qualifications and methodology regarding his testimony on the safety and efficacy of the TVT and Prolift designs.[4] In his Prolift report in this litigation, Dr. Grier includes a section titled "VI. The Design of Prolift" with a subsection titled "The Usefulness, Desirability, and Safety of the Prolift Device."[5] In this section, Dr. Grier offers expert opinions about specific design features of the Prolift device which contribute to the safety of the device.[6] For example, in this section, Dr. Grier opines that specific mesh design properties, such as the "lightweight, large-pore, knitted, monofilament" mesh contribute to the safety of the mesh.[7] Dr. Grier's opinions regarding the safety and efficacy of the design of the Prolift and TVT mesh should be excluded for the reasons stated in Plaintiffs' original Memorandum. To the extent necessary, the Plaintiffs incorporate their Wave 1 Memorandum as Exhibit A.

II. In Wave 1 this Court excluded Dr. Grier's expert testimony about product warnings and the result here should be the same.

This Court recently excluded Dr. Grier's expert testimony about product warnings, which includes expert testimony about the adequacy of the relevant IFU. Mem. Op. and Order (*Daubert* Motion re: Douglas Grier, M.D.), No. 2:12-md-02327, at 7-8 (S.D. W. Va. Aug. 31, 2016) [ECF # 2703] ("Dr. Grier does not possess the additional expertise to offer expert testimony about what an IFU should or should not include. Accordingly, Dr. Grier's expert

[3] *Id.* at 7.
[4] Ethicon has stated that "[t]o the extent Plaintiffs challenge Dr. Grier's qualifications and methodology regarding his testimony on the *safety* and *efficacy* of the TVT and Prolift designs, Ethicon incorporates and adopts its Opposition to Plaintiffs' Wave 1 motion." Defs' Brf. at 2.
[5] Ex. B, Dr. Grier Prolift Report at 22-24; *see also* Ex. C, Dr. Grier TVT and TVT-O Report at 25-30.
[6] *Id.*
[7] *Id.*

testimony about these matters is **EXCLUDED**."). The Court's ruling here should be no different.

In excluding Dr. Grier's warnings testimony, this Court noted that "[w]hile an expert who is a urologist *may* testify about the specific risks of implanting mesh and whether those risks appeared on the relevant IFU, the same expert *must possess additional expertise* to offer expert testimony about what information should or should not be included in an IFU."[8] The Court has carefully considered Dr. Grier's qualifications about product warnings and found that he does not possess the expertise to offer testimony about what risks should be included in a product IFU.[9] Ethicon's Response Memorandum has not identified any new qualifications or expertise possessed by Dr. Grier since the Court last considered this issue.[10] As such, Dr. Grier's proposed expert testimony regarding product warnings, which includes expert testimony about the adequacy of the relevant IFUs should be excluded. To the extent necessary, the Plaintiffs incorporate their Wave 1 Memorandum as Exhibit A.

CONCLUSION

For reasons of the forgoing, the opinions of Dr. Grier, as set forth herein, must be excluded as they do not meet the standard governing expert opinion set forth by federal law.

Date: October 18, 2016.

By: /s/ Edward A. Wallace
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[8] Mem. Op. and Order (*Daubert* Motion re: Douglas Grier, M.D.), No. 2:12-md-02327, at 7-8 (S.D. W. Va. Aug. 31, 2016) [ECF # 2703] (emphasis added).
[9] *Id.*
[10] Defs' Brf. at 2-5.

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CERTIFICATE OF SERVICE

I hereby certify that on October 18, 2016, I electronically filed the foregoing document with the Clerk of the court using CM/ECF system which will send notification of such filing to the CM/ECF participants registered to receive service in this MDL.

/s/ Edward A. Wallace

Exhibit A

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON DIVISION

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	**Master File No. 2:12-MD-02327** **MDL 2327** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**
THIS DOCUMENT RELATES TO: **Ethicon Wave 1 cases listed in Exhibit A**	

PLAINTIFFS' MEMORANDUM IN SUPPORT OF THEIR MOTION TO EXCLUDE CERTAIN OPINIONS AND TESTIMONY OF DOUGLAS GRIER, M.D.

Plaintiffs respectfully request that the Court preclude defense expert Douglas Grier, M.D., a urologist, from giving opinions on (1) the design of Defendants' transvaginal mesh products at issue, including the safety and efficacy of those devices; (2) his statements about the safety and efficacy of Defendants' products based on his own practice; and (3) the adequacy of Defendants' product warnings and instructions for use ("IFU").

LEGAL STANDARD

Federal Rule of Evidence 702 sets forth the basic framework for analyzing the admissibility of expert opinions. The rule reads, in pertinent part, as follows:

> If scientific, technical, or other specialized knowledge will assist the trier of fact to understand the evidence or to determine a fact in issue, a witness qualified as an expert by knowledge, skill, experience, training, or education, may testify thereto in the form of an opinion or otherwise, if (1) the testimony is based upon sufficient facts or data, (2) the testimony is the product of reliable principles and methods, and (3) the witness has applied the principles and methods reliably to the facts of the case.

Fed. R. Evid. 702. On the issue of qualifications, "the district court must decide whether the expert has 'sufficient specialized knowledge to assist the jurors in deciding the particular issues

in the case.'" *Belk, Inc. v. Meyer Corp., U.S.*, 679 F.3d 146, 162 (4th Cir. 2012), *as amended* (May 9, 2012) (quoting *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 156 (1999)).

If the witness is suitably qualified, then the *Daubert* inquiry generally breaks down into a two-step analysis. The first issue is whether the proffered evidence represents "scientific knowledge," meaning that it is supported by appropriate validation. The second issue is whether the evidence would assist the jury—i.e., whether it is relevant. *United States v. Dorsey*, 45 F.3d 809, 813 (4th Cir. 1995). The relevance aspect of the inquiry is often discussed in terms of whether the expert's opinions "fit" the case. *See Daubert v. Merrell Dow Pharms., Inc.*, 509 U.S. 579, 591-92 (1993).

To meet the standard of reliability, the testimony "must be supported by appropriate validation—i.e., 'good grounds,' based on what is known. In short, the requirement that an expert's testimony pertain to 'scientific knowledge' establishes a standard of evidentiary reliability." *Benedi v. McNeil-P.P.C., Inc.*, 66 F.3d 1378, 1383 (4th Cir. 1995).

There are five factors courts often consider, taken from the *Daubert* opinion, in assessing the reliability of expert testimony:

- (1) whether the testimony has been tested,
- (2) whether it has been published or exposed to peer review,
- (3) its rate of error,
- (4) whether there are standards and controls over its implementation, and
- (5) whether it is generally accepted.

See Cavallo v. Star Enterprise, 100 F.3d 1150, 1158 (4th Cir. 1996). However, "the factors discussed in *Daubert* were neither definitive, nor exhaustive." *Cooper v. Smith & Nephew, Inc.*, 259 F.3d 194, 199 (4th Cir. 2001).

Courts should focus on expert witnesses' "principles and methodology, not on the conclusions that they generate." *Md. Cas. Co. v. Therm-O-Disc, Inc.*, 137 F.3d 780, 783 (4th Cir. 1998). This is because "*Daubert* governs whether evidence is admitted, not how persuasive it must be to the factfinder." *Cavallo*, 100 F.3d at 1158.

ARGUMENT

This Court should prohibit Dr. Grier from giving the opinions referenced above because he is not qualified to opine on those issues and has not done the necessary research to produce opinions that can reliably be applied to this case.

Dr. Grier has issued four lengthy reports in this litigation addressing the following five products: TVT and TVT-O, TVT-S, Prolene Soft and Prolift (the "subject products"). All of these reports contain the same general opinions/statements:

- The products at issue were not defective, were reasonably safe for their intended use, and had a positive benefit-to-risk profile. Dr. Grier opines that the benefits of Defendants' products outweigh the risks of using them, and each product is safer and better than non-mesh alternatives. The products could not have been made safer for their intended uses at the time they were launched, and the products were state of the art when launched. (Prolift Report, attached as Exhibit B, at 24; Prolene Soft Report, attached as Exhibit C, at 19; TVT/TVT-O Report, attached as Exhibit D, at 29; TVT-S Report, attached as Exhibit E, at 34-35).
- Dr. Grier opines about his experience in his own practice related to the safety and efficacy of Defendants' product at issue. (*See, e.g.*, Prolift Report, Ex. B, at 15-16; Prolene Soft Report, Ex. C, at 11-12; TVT/TVT-O Report, Ex. D, at 13-14).

- The IFU and/or the warnings concerning Defendants' subject product are adequate and allow for the safe use of the device. (Prolift Report, Ex. B, at 20; Prolene Soft Report, Ex. C, at 16; TVT /TVT-O Report, Ex. D, at 22; TVT-S Report, Ex. E, at 28).

The first bullet point does not use the word "design," but it clearly is an opinion about the subject products' design. The first point recites the legal test on a design defect claim in West Virginia. *See Morningstar v. Black & Decker Mfg. Co.*, 253 S.E.2d 666, 683 (W. Va. 1979) (stating that "the general test for establishing strict liability in tort is whether the involved product is defective in the sense that it is not **reasonably safe for its intended use**" (emphasis added)). The second clause addresses the risk-utility test, which the focus of the design defect inquiry in many states. *See, e.g.*, *Beard v. Johnson & Johnson, Inc.*, 41 A.3d 823, 836 (Pa. 2012); *Branham v. Ford Motor Co.*, 701 S.E.2d 5, 14 (S.C. 2010); *Mikolajczyk v. Ford Motor Co.*, 901 N.E.2d 329, 352 (Ill. 2008), *opinion modified on denial of reh'g* (Dec. 18, 2008); *Hernandez v. Tokai Corp.*, 2 S.W.3d 251, 258 (Tex. 1999); *Halliday v. Sturm, Ruger & Co.*, 792 A.2d 1145, 1150 (Md. Ct. App. 2002); *Cavanaugh v. Skil Corp.*, 751 A.2d 564, 580 (N.J. Super. App. Div. 1999), *aff'd*, 751 A.2d 518 (N.J. 2000). The next point addresses the utility of alternative designs, which generally factor into the design defect analysis in some manner. *See, e.g.*, *Branham*, 701 S.E.2d at 14; *Hernandez*, 2 S.W.3d at 258; *Halliday*, 792 A.2d at 1150.

The second bullet point relates to Dr. Grier's attempt to bolster his design defect opinion based on his own experience as to the safety and efficacy of Defendants' products. As discussed in greater detail below, this is Dr. Grier's attempt to backdoor into evidence an improper and unsupported opinion on his personal complication rate.

The final bullet point contains an opinion expressly directed to the adequacy of the warnings and IFU accompanying the subject products.

For the reasons described below, Dr. Grier should not be permitted to give those opinions under the standards set by Rule 702 and *Daubert*.

I. Dr. Grier should be precluded from giving design opinions.

a. Dr. Grier expressly testified he is not a design expert.

The first reason, and perhaps the most important reason, that Dr. Grier should be precluded from opining about the design of the subject products is that he admits he is not an expert on design:

> Q (By Mr. DeGreeff) Let's try this again. Doctor, yes, no, or you cannot answer my question as it's phrased: Are you holding yourself out as an expert in the design of transvaginal mesh products?
>
> MR. KOOPMANN: Same objection.
>
> THE WITNESS: No, I'm not a design expert.

(March 22, 2016 Deposition of Douglas Grier ("Grier Deposition"), portions attached as Exhibit F, at 68:21-69:2).

> Q Are you qualified to give -- you're not holding yourself out as an expert on the area of design, are you?
>
> MR. KOOPMANN: Objection to form.
>
> THE WITNESS: No.
>
> Q (By Mr. DeGreeff) I mean, you've never designed a medical device; correct?
>
> A Correct.

(*Id.* at 128:22 – 129:3).

> Q You don't have any patents on medical devices?
>
> A No.

(*Id.* at 129:7-8).

Even during defense counsel's attempt to rehabilitate him, Dr. Grier once again confirmed his lack of design expertise:

Q You don't hold yourself out to the community as a design expert; is that fair?

A That is fair.

(*Id.* at 329:3-5).

This Court has previously recognized the importance of an expert's admission that he is not an expert. In the *Bard* litigation, this Court precluded Dr. Shull from giving warnings opinions because he had testified that "I would not claim to be an expert in that area." *In re C.R. Bard, Inc.*, 948 F. Supp. 2d 589, 611 (S.D.W. Va. 2013), *amended on reconsideration in part* (June 14, 2013). That same analysis applies here to Dr. Grier, who admitted on multiple occasions during his recent deposition that he is not an expert on design. As such, he should be precluded from giving any opinions related to design of the subject products.

b. Dr. Grier did not review Defendants' key documents related to product design, and even if he had reviewed them Dr. Grier has no base of knowledge as to what those documents would demonstrate.

Dr. Grier should also be precluded from opining about the design of the subject products because he has not reviewed Defendants' internal documents about the design process. In the Boston Scientific litigation, Boston Scientific Corp. ("BSC") moved to exclude Dr. Shull because he "reached opinions on the improper design of the Uphold without having first considered BSC's design protocols." *Winebarger v. Boston Scientific Corp.*, No. 2:13-CV-28892, 2015 WL 1887222, at *14 (S.D. W. Va. Apr. 24, 2015). The plaintiffs countered that Dr. Shull had relied on other BSC internal documents, as well as the scientific literature. *Id.*

This Court agreed with BSC and excluded Dr. Shull from giving any design opinions. This Court reasoned that "regardless of the literature he has reviewed or the experience he has

gained, a necessary piece of data remains missing from Dr. Shull's methodology. Without any reliable, demonstrated knowledge of BSC's internal design procedures, Dr. Shull cannot substantiate his opinion that these procedures were (1) departures from the norm; (2) not followed by BSC; or (3) lacking in any way." *Id.*

The same analysis applies to Dr. Grier in this case. He confirmed repeatedly that he did not review Defendants' internal design documents in formulating his opinions because he did not find them "relevant":

> Q (By Mr. DeGreeff) Did you -- in rendering your opinions, did you rely at all on internal company documents?
>
> A No.
>
> Q Why not?
>
> A I don't find them necessarily relevant.
>
> Q Why are they not relevant?
>
> A Well, because a lot of it has to do with research and development early on in the development of the products, and quite frankly, it's not -- I don't find it relevant for me in rendering an opinion.

(Grier Deposition, Ex. F, at 43:17 – 44:1).

> Q So my question is about design documents that would be relevant to the products that we're here about. Do you remember reviewing any of those design documents?
>
> A Not specifically.

(*Id.* at 45:10-13).

> Q Okay. So my question was a little different than that. Have you reviewed -- and I don't care when you reviewed them. Have you reviewed all of the … documents that are in that binder?
>
> A Well, no. The ones I haven't reviewed were the pre-FDA design documents, which are very tedious, and I didn't find relevant.

Q So fair to say, you did not review the design documents that were relied on by Ethicon for approval by the FDA?

MR. KOOPMANN: Objection to form.

THE WITNESS: That's true.

Q (By Mr. DeGreeff) Anything else?

A Well, there's just a bunch of minutes and discussions by, I guess, engineers within the—within the company on the product specifications and the launch of the product.

Q And did you review those?

A I did not.

Q Why not?

A Well, because I don't find it relevant.

Q And that's the—those are memos done by the engineers who designed the product?

A Correct.

Q Why did you not find that relevant?

A Well, because it's tremendously tedious, and it's not clinically relevant. It was how they developed the product and—the device, and it's kind of too technical for my interest.

Q And you didn't—so you didn't review that in rendering your opinions?

A No.

(Grier Deposition, Ex. F, at 65:8-66:12). In fact, he did not review Defendants' internal documents globally because he did not find them relevant. (*Id.* at 316:5-13). Because he did not review the relevant design documents, Dr. Grier lacks the required knowledge to give a reliable opinion about the design of Defendants' transvaginal mesh products.

Moreover, Dr. Grier conceded that he could not recall reviewing the design history file for Defendants' products:

Q Well, have you reviewed the design device file?

MR. KOOPMANN: Objection. Form.

THE WITNESS: I don't recall.

(Grier Deposition, 44:17-19). As the name suggests, the design history file would include all of the information about the design of the product. The necessary components of a design history file are laid out in 21 C.F.R. § 820. *See* 21 C.F.R. § 820.1 ("The requirements in this part govern the methods used in, and the facilities and controls used for, the design, manufacture, packaging, labeling, storage, installation, and servicing of all finished devices intended for human use."). Defendants' research and design engineer Katrin Elbert, Ph.D., testified that the design history file is "the archive of all the documents that show us the history of the design of the product. It contains all of our design control documents, and it's also what we use to support regulatory submissions." (12-23-14 Elbert Dep., portions attached as Exhibit G, at 270:5-11). Dr. Grier's failure to review such important documents leaves him without a reasonable foundation for opinions about the design of the subject products. In addition, Dr. Grier had not heard of MedScand, which is the company that partnered with Ulf Ulmsten in developing the TVT, one of the subject products. (Grier Deposition, Ex. F, at 129:15-17).

Dr. Grier also confirmed he has not read the failure modes and effects analysis for the subject products, has never been involved in one, does not believe those analyses to be pertinent evidence, and does not know what that phrase means. (Grier Deposition, Ex. F, at 135:19 – 137:3, 138:5-19, 331:9-11). As discussed in the deposition of Defendants' medical director Charlotte Owens, the purpose of a design failure modes and effects analysis ("dFMEA") is to

"review the potential risk associated with the design of the product." (9-13-12 Owens Dep., portions attached as Exhibit H, at 485:14-24).[1]

> Q. And when you say "associated with the design of the product," that means that when the product is in a woman's body and the product was manufactured completely consistent with the specifications, these are the things that could go wrong and harm a patient, correct?
>
> A. Correct.

(*Id.* at 485:25-486:7).

> Q. And you understood that it was required that you capture all of the different failure modes, all the things that could go wrong in the procedure, even if the doctor was properly trained and following the proper procedure, and the effects of those failure modes, the hazards that could occur, and the resulting harms, and you were supposed to capture all of them, correct?
>
> A. Yes, all that we could conceive of, yes.

(*Id.* at 449:12-22). Dr. Grier should have reviewed these documents in forming his opinions about the design of the subject products; but not only did he fail to review those documents, he did not even know what the phrase "failure modes and effects analysis" means.

All this being said, even if Dr. Grier had reviewed the relevant design documents, he does not even know what product design documents are:

> Q Well, do you know what I'm talking about when I say design documents?
>
> A Not precisely, no.

(Grier Deposition, Ex. F, at 44:12-14). Given this fact, he would not have been able to interpret and use those documents in rendering opinions regardless of whether he read them. This is confirmed by his testimony that the design documents are "tedious" and "too technical for his interest." (*Id.* at 66:5-9).

[1] Ms. Owens's cited deposition related to the Prolift product only, but the discussion quoted was not product-specific.

Based on the foregoing, Dr. Grier's opinions on the issue of product design should be excluded.

II. Dr. Grier's statements about his personal experience related to the safety and efficacy of the subject products should be excluded because he has kept no records on those points, and this information exist only in his mind.

Dr. Grier should be precluded from testifying about his perceived safety and efficacy rates with the subject product from his own practice, as that information exists only in Dr. Grier's head and is entirely unsupported by any statistical information/analysis. As an example, Dr. Grier's Prolift report includes the following statement:

> I have personally performed over 1,000 procedures involving implantation of Prolene polypropylene mesh for treatment of stress urinary incontinence or pelvic organ prolapse, and have found the Prolene polypropylene products to be safe and efficacious when following the appropriate patient selection and the technique described by the product instructions for use and sound medical judgment and surgical technique and concepts … . The devices are high quality, straightforward, and the polypropylene mesh is stable over time, as I have patients implanted 15 years ago and see no long-term complication trends … . The overwhelming majority of those anxious patients have excellent outcomes and no adverse symptoms.

(Grier Prolift Report, Ex. F, at 15-16). Defendants have now caught on to the fact that their experts' opinions about complications rates among their own patients are inappropriate, unsupported and inadmissible, so Dr. Grier now seeks to backdoor essentially the same opinion by excluding a precise complication rate. This should not be permitted, as Dr. Grier lacks any data or analysis to support his conclusions:

> Q So do you have something in your office where you track the reason for each removal and what product it is you're removing?
>
> A Their medical records.
>
> Q Is that a list you would keep in your office somewhere?
>
> A It's one I could retrieve.

Q So you have a list currently kept in your office of the product you removed and with -- with the reason for removal?

A No, I don't have a list.

(Grier Deposition, Ex. F, at 143:10-19).

Q That was going to be my question. Where's the tracking data on TVT-Rs that were removed, on the number of explants you've done?

A What do you mean by "tracking data"?

Q Is that something you keep track of in your office?

A No, I don't keep track of the numbers.

(*Id.* at 144:14-19).

Q Doctor, do you do anything within your office to track what percentage of the women that you do implants in are lost to follow-up?

A No.

….

Q And a lot of patients aren't comfortable going back to the person who put in an implant that gave them complications; fair?

A That's -- complications in general, for all of medicine, a lot of times patients have unrealistic expectations and will go elsewhere when they don't have exactly the outcome that they want. That's very common, not just in this.

Q Okay.

A It's common with all complications.

(*Id.* at 146:12-15, 147:6-15).

Q And what was the point of this email? What was – what were you trying to tell her with that?

A I was -- I saw a rolling -- a rolling average of what I had spent for slings, and so I was kind of shocked by that number. I can't remember what they cost, but that's the equivalent of 100 -- probably 100 slings -- surgeries.

> So I -- just like I don't count what -- what I've been paid, I normally don't count how many slings that I've done in a given year. And so this was toward the end of the year, and it looks like I did 100 slings.

(*Id.* at 268:18 – 269:3).

This testimony speaks for itself. Dr. Grier is asserting and relying on alleged safety and efficacy data from his own practice, and yet he has no foundation whatsoever for that assertion. He does not track the reason for removal or the transvaginal mesh product removed, the number of removals for various products, the total number of transvaginal mesh implants he performs, or the percentage of the patients in whom he implanted transvaginal mesh products that are lost to follow up (i.e. go to another doctor for removal). As such, any estimates about safety rates from Dr. Grier's practice are extremely unreliable, and Plaintiffs have no reasonable way of testing the veracity of his claims, which exist only in his mind. Because there is no foundation for this testimony, Dr. Grier should be prohibited from providing this testimony. Allowing him to do so would be akin to permitting an improper opinion about his personal complication rates.

III. Dr. Grier admits that he has no expertise in the area of warnings and IFUs, and his opinions on those issues should be excluded.

As discussed in Section I, above, this Court has recognized the importance of an expert's admission that he is not an expert in the area of warnings. *In re C.R. Bard, Inc.*, 948 F. Supp. 2d at 611. Just like his design opinions, Dr. Grier's opinions concerning the adequacy of the warnings and IFUs for the subject product should be excluded because he admits he is not an expert:

> Q Doctor, you're not an expert on warnings, are you?
>
> MR. KOOPMANN: Objection. Form.
>
> Q (By Mr. DeGreeff) Medical device warnings?
>
> MR. KOOPMANN: Same objection.

THE WITNESS: No.

(Grier Deposition, Ex. F, at 127:25 – 128:4). Dr. Grier confirmed this again during defense counsel's attempt to rehabilitate him:

> Q And you don't hold yourself out to the community as a warnings expert; correct?
>
> A No, I don't.

(*Id.* at 329:11-13). Additionally, Dr. Grier did not review the November 2015 deposition of the 30(b)(6) witness chosen by the Defendants to testify on the revised IFUs for their products. (*Id.* at 356:5-19).

Dr. Grier has clearly admitted he is unqualified to give opinions on the adequacy of Defendants' warnings and IFUs, and has failed to the proper research necessary to give those opinions. Therefore, Dr. Grier's opinions on this issue should be precluded.

CONCLUSION

Based on the foregoing, Dr. Grier should be precluded from giving opinions on (1) the design of Defendants' transvaginal mesh products at issue, including the safety and efficacy of those devices; (2) his statements about the safety and efficacy of Defendants' products based on his own practice; and (3) the adequacy of Defendants' product warnings and IFUs.

Dated: April 21, 2016

Respectfully submitted,

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CERTIFICATE OF SERVICE

I hereby certify that I filed the foregoing document on April 21, 2016, using the Court's CM-ECF filing system, thereby sending notice of the filing to all counsel of record in this matter.

/s/Thomas P. Cartmell
Attorney for Plaintiffs

Exhibit B

Report re Prolift

Douglas H. Grier, M.D.
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This report contains a summary of my qualifications, education, training, and experience, a statement of my opinions that I have formed to date, the bases for those opinions, and the information I considered in forming my opinions. All of my opinions are based on my education, training, clinical experience, the pertinent medical literature, discussions with colleagues, and other materials I have reviewed. Materials that support my findings and opinions, including documents that I have reviewed, are identified either in this report or are listed in the attached reliance materials list.

All of the opinions I express in this report are held to a reasonable degree of medical and scientific certainty. If I receive additional information after signing this report but before trial, I may form additional or different opinions.

I. Background

a. Education, Training, and Experience

I attended the University of Florida in Gainesville, Florida, graduating with a Bachelor of Science degree in Chemistry with High Honors in 1976. I attended medical school at George Washington University, graduating in 1982. I then did a surgical internship in 1982–1983 at the Portsmouth Naval Hospital in Portsmouth, Virginia. Following my internship, I did a urological residency at the Portsmouth Naval Hospital from 1984–1988. I served as Chief of Urology at Jacksonville Naval Hospital in 1990-91.

Prior to my residency, I served in Operation Urgent Fury in Grenada in October 1983 and as part of the Multinational Peacekeeping Force in Beirut, Lebanon in 1983–1984. After my residency, I served in Operation Desert Shield and Operation Desert Storm with the 1st Marine Division, stationed in Saudi Arabia and Kuwait in 1990–1991.

I am the President-Elect of the Medical Staff at Swedish/Edmonds Hospital in Edmonds, Washington. I also serve as the Chair of Swedish Hospital's Medical Quality Oversight Committee, Chair of the Credentials Committee, Treasurer of the Medical Staff for the Swedish Hospital System, and as a member of the Executive Committee at Swedish Hospital.

I became a Diplomate of the American Board of Urology in 1990 and was recertified in 2010. I am an active member of the American Urological Association, the Washington State Medical Association, the Northwest Urological Society, the Washington State Urology Society, the King County Medical Society, the American Association of Clinical Urologists, the Society of Urodynamics Female Pelvic Medicine & Urogenital Reconstruction, and the International Continence Society.

My curriculum vitae is attached to this report.

b. Clinical Experience & Personal Experience with Stress Urinary Incontinence and Pelvic Organ Prolapse Treatments

I have a special focus in female pelvic medicine and surgery. Over the course of my career, I have performed various types of native tissue surgery and surgery utilizing mesh, including Ethicon's TVT and TVT-O, TVT-Abbrevo, and TVT-Secur mid-urethral slings, AMS Monarch, Uretex by Bard, Vesica In situ sling, Stamey cystourethropexy, MMK, and Burch procedures. I have also performed robotic sacrocolpopexies, as well as open abdominal sacrocolpopexies. I have also performed various types of native tissue surgeries and surgeries utilizing mesh—including the Prolift device—to treat pelvic organ prolapse.

c. Teaching & Training Experience Related to Stress Urinary Incontinence

I served as a faculty member at the Ethicon Endosurgical Institute, and as a National Preceptor for Gynecare products, conducting over 300 courses for advanced surgical training of physicians for conditions such as stress urinary incontinence and pelvic organ prolapse. I have lectured to pelvic floor surgeons throughout the United States, Canada, Europe, and China. I have performed research in the field of incontinence and bladder disorders, contributing to studies on the use of TVT abdominal guides, and the TVT world registry published in the Journal of Urology in 2011. I was also an investigator in an FDA trial of a pelvic nerve stimulator for the treatment of urge incontinence.

d. Litigation Consulting Work

During the previous four years, I have testified as an expert witness at trial or by deposition in the following case:

- Perry v. Ethicon, Inc., et al.—Bakersfield, CA
  - Deposition Testimony on 12/30/14
  - Trial Testimony on 02/17/15, 02/18/15, and 02/19/15

I am being compensated $500 per hour for my study and testimony in this case.

IV. Pelvic Organ Prolapse

a. Definition, Mechanism of Action, and Prevalence

Pelvic organ prolapse, overactive bladder, and urinary incontinence affect more women than diabetes, heart disease, or arthritis. The overall lifetime risk for undergoing surgery for pelvic organ prolapse is 11.1% or 1 in 9 women by the age of 80. The risk of surgery increases to 16% status post hysterectomy.

The proposed mechanism of action for the development of pelvic organ prolapse begins with damage to the levator ani muscles and nerves which decreases muscle tone and strength,

leading to muscular disuse atrophy causing descent and a widened levator hiatus. Increased intra-abdominal pressure is then unopposed, placing additional forces on the connective tissue, which stretches and tears over time. Pelvic organ prolapse is most common in the anterior compartment and then posterior compartment, with apical prolapse the least common as a site-specific defect.

b. Risk Factors for Stress Urinary Incontinence

Smoking: Women who smoke have a 2-3 times more likely incidence of urinary incontinence chronic obstructive pulmonary disease and increasing abdominal pressures causing pelvic organ prolapse.

Obesity: Increasing body mass index correlates to an increase in the symptoms of urinary incontinence and pelvic organ prolapse.

Menopause: Decreasing serum levels of estrogen are known to increase the incidence of both stress incontinence and decrease the integrity of the pubocervical fascia of the vagina by decreasing vascularity and thickness of the tissues. Postmenopausal decreased estrogen levels lead to urogenital atrophy with the increased risk of infections of the urinary tract and changing of the vaginal pH.

Pregnancy and Childbirth: Damage sustained to the muscles and nerves of the pelvic floor significantly increase the risk of both stress and urge incontinence and pelvic organ prolapse. There is an 11-fold increased risk of pelvic organ prolapse with three or more vaginal deliveries compared to nulliparous women. The weight of the infant contributes to prolapse with an increase of 10% per pound weight of the infant.

Race: Increasing incidence of prolapse occurs from African-American < Asian<Caucasian<Hispanic. Hispanic women have the highest risk of pelvic organ prolapse

Age: Pelvic organ prolapse levels increase with each decade for women between the ages of 20 and 59 years and the incidence of prolapse requiring surgery also has a dramatic increase with each successive decade.

Congenital factors: Women with prolapse having an abundance of the weak or type III collagen in the pubocervical fascia with a higher degree of joint hypermobility with associated collagen vascular disorders also increase the incidence and severity of prolapse.

Hysterectomy: The lifetime risk of prolapse post-hysterectomy is 16% with no specific technique increasing risk. The incidence of women developing severe prolapse after hysterectomy is to 3.6 birth 1000 women years and if the hysterectomy was performed with initial complaints of prolapse or rate is as high as 15 per 1000 women years.

Stress Urinary Incontinence: 62% of women with prolapse also report stress incontinence, and 63% of women with stress incontinence have associated prolapse. 30% of women will undergo repeat surgery for recurrent prolapse over their lifetime.

V. Treatment Options for Pelvic Organ Prolapse

a. Nonsurgical Options for Treatment of Pelvic Organ Prolapse

Conservative management of pelvic organ prolapse is the avoidance of pelvic and abdominal straining in the form of heavy lifting or squatting. Patients can also be treated with physical therapy using biofeedback, Kegel exercises, estrogen vaginal supplementation, and pessaries.

b. Surgical Options for Treatment of Pelvic Organ Prolapse

Surgical corrections of pelvic organ prolapse have many different approaches—from either vaginal or retropubic—and involve open incisions or laparoscopic techniques. For relatively simple cystocele and rectocele repair, native tissue plication with absorbable sutures can be provided, but has a 30-50% 5-year failure rate based on multiple studies. Sacrospinous ligament fixation and uterosacral ligament repairs have higher rates of success, but also higher rates of complications including chronic pelvic pain, dyspareunia, urinary retention, and injury to adjacent organs such as the bladder, rectum, and vessels. Retropubic abdominal sacrocolpopexy performed either open or laparoscopically is also an option. It has the highest rate of success but also a significant rate of complications.

Due to the high rate of failure using native tissue plication and suture fixation, biologic and synthetic materials have been incorporated into repairs for over 30 years. Cadaveric fascia, autologous fascia, or synthetic meshes have been incorporated to augment the repair in an attempt to increase the anatomic long-term success. The augmented repairs have the same potential complications as native tissue plications, with additional possible complications of mesh exposure, extrusion, or perforation of adjacent organs. The rate of vaginal mesh exposure varies from 3% to 34% in various studies, and with small areas of exposure topical estrogen and time may be all that is required for treatment. For larger areas of exposure or pain, local excision can be performed using either local anesthetic or general anesthesia. Mesh excision can be performed in the office setting, or an outpatient surgery center, as well as hospitals.

Maher and colleagues analyzed 56 randomized controlled trials evaluating 5,954 women with the objective of determining "the effects of the many different surgeries used in the management of pelvic organ prolapse." They studied 21 trials that compared various surgical procedures for treating cystocele and found that traditional anterior prolapse repair was associated with more anterior compartment prolapse than any polypropylene mesh repair. They found that patients were more aware of their prolapse after anterior native tissue repairs than were patients receiving a polypropylene mesh repair.[1] Weber and colleagues, in 2001, conducted a randomized controlled trial studying three surgical techniques for anterior colporrhaphy and found that only 30% of the patients in the standard anterior colporrhaphy

[1] Maher C, et al., Surgical management of pelvic organ prolapse in women, Cochrane Review 2013.

group had satisfactory or optimal anatomic results, compared to 42% in the standard plus mesh group and 46% in the unilateral anterior colporrhaphy group.[2]

Barber and colleagues showed that the success rates of sacrospinous ligament fixation and uterosacral ligament fixation were nearly equal at 60.5% and 59.2%, respectively.[3] Failure of native tissue repairs is common and can occur when sutures break, pull through the tissue, or are prematurely absorbed.

c. Pelvic Organ Prolapse's Economic Impact and Impact on Quality of Life

Pelvic organ prolapse can have significant adverse effects on the quality of women's lives. It can be painful, can negatively affect women's relationships, and it can cause patients to isolate themselves socially and be less active. Symptoms include a feeling that something is falling out of the vagina, a pulling sensation in the pelvic area, lower back pain, and a sensation of pressure of fullness from organs pressing against the vaginal walls. Patients with rectocele often have constipation as a result. The costs of pelvic organ prolapse surgery was calculated to be over a billion dollars in 1997.[4]

IV. Ethicon's Prolift Device

a. Historical Background of Surgical Use of Mesh

Polypropylene monofilament suture was introduced into surgery in 1958 by Usher, and has become the main material used in tissue repair. Polypropylene sutures have been used for over 55 years and are biologically compatible with human tissue. Polypropylene hernia mesh has been and continues to be the standard of care for the last thirty years for abdominal wall hernia repair. Polypropylene mesh has been used in open abdominal sacrocolpopexies since the 1960s. The advantage of mesh is augmentation and strength during the healing process with the incorporation of collagen fibers into the material to provide lasting support. I have been performing polypropylene mesh hernia repairs since the 1980s and have never had a patient develop an infection or rejection of the material.

Polypropylene meshes have been used in the vagina for almost 60 years. Surgeons have turned to synthetic materials to augment healing and reinforcement of poor-quality native fascia and collagen that has deteriorated both by years and trauma of parity. Due to the high failure rate of suture repairs for vaginal prolapse, mesh grafts have been developed to address the problem in the same manner as hernia repairs of the abdominal wall.

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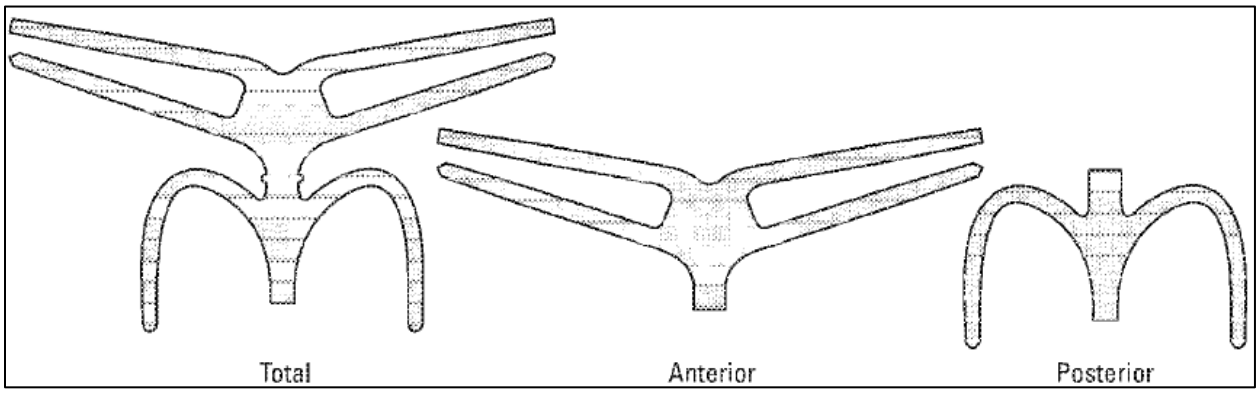
[2] Weber AM, et al., Anterior colporrhaphy: A randomized trial of three surgical techniques. Am J Obstet Gynecol 2001 Dec. 185(6):1299–1306.
[3] Barber MD, et al., Comparison of 2 Transvaginal Surgical Approaches and Perioperative Behavioral Therapy for Apical Vaginal Prolapse – The OPTIMAL Randomized Trial. J Am Med Assoc 2014;311(10):1023–1034.
[4] Subak LL, Cost of pelvic organ prolapse surgery in the United States. Obstet Gynecol 2001 Oct;98(4):646–51.

b. The Development of the Prolift Device

Due to the high failure rates of native tissue repairs like colporrhaphies, the morbidity of open abdominal sacral colpopexy, the high failure rate and infection rates associated with biologic grafts, surgeons began using transvaginal mesh to treat pelvic organ prolapse. In 2000, a group of surgeons in France calling themselves the "TVM Group" started to study the use of non-absorbable synthetic mesh in urogenital prolapse repair, which was prompted by the 20–30% prolapse recurrence rates following traditional native tissue repairs. The TVM Group selected Prolene Soft mesh, as they found it to be the most appropriate mesh for the transvaginal approach of the surgical repair of prolapse. They noted that the Prolene Soft was "a carefully selected and tested synthetic material."[5]

In 2002, Gynemesh™ PS was introduced, and was "indicated for tissue reinforcement and long-lasting stabilization of fascial structures of the pelvic floor in vaginal wall prolapse where surgical treatment is intended, either as mechanical support or bridging material for the fascial defect." It was the first synthetic polypropylene mesh indicated for pelvic floor repair.

The Prolift device was introduced in March 2005. The Prolift device consists of pre-cut Gynemesh PS non-absorbable mesh implants and a set of instruments to facilitate mesh placement. It is implanted via a procedure "designed for and by surgeons."[6] The Prolift Total system consisted of an anterior and posterior implant had six straps—four for securing the anterior portion of the implant via a trans-obturator approach, and two straps for securing the posterior portion of the implant in the sacrospinous ligament via a trans-gluteal approach.



The Prolift system also included a Guide, Cannula, and Retrieval Device to facilitate passage and placement of the implant straps while protecting the surrounding tissue. It is inserted transvaginally, through a full-thickness vaginal incision. The mesh is placed through the arcus tendineus fascia pelvis (ATFP) or the sacrospinous ligament (SSL), and is placed tension-free.

The Gynemesh PS used in the device is a monofilament, knitted, macroporous, synthetic mesh. It is made of knitted filaments of extruded polypropylene identical in composition to that

[5] Berrocal J, et al., Conceptual advances in the surgical management of genital prolapse—The TVM technique emergence. J Gynecol Obstet Biol Reprod 2004;33:577–87.
[6] Prolift Surgeon's Resource Monograph.

used in Prolene polypropylene sutures that have been used in various surgical specialties for more than 50 years, and it includes blue Prolene monofilaments to produce contrast striping that makes the mesh more visible when implanted. The Prolift IFU notes that "[t]he mesh is constructed of reduced diameter monofilament fibers, knitted into a unique design that results in a mesh that is approximately 50 percent more flexible than standard PROLENE mesh." The knitting process provides for elasticity in both directions—which "allows adaptation to various stresses encountered in the body." The IFU also notes:

> Animal studies show that implantation of GYNECARE GYNEMESH PS mesh elicits a minimal to slight inflammatory reaction, which is transient and is followed by the deposition of a thin fibrous layer of tissue which can grow through the interstices of the mesh, thus incorporating the mesh into adjacent tissue. The mesh remains soft and pliable, and normal wound healing is not noticeably impaired. The material is not absorbed, nor is it subject to degradation or weakening by the action of tissue enzymes.

The mesh is a Type I mesh, per the biomaterial classification published by PK Amid in 1997, as it contains pores larger than 75 microns, "which is the required pore size for admission of macrophages, fibroblasts (fibroplasia), blood vessels (angiogenesis) and collagen fibers into the pores." (Amid PK, Classification of biomaterials and their related complications in abdominal wall hernia surgery. Hernia 1997;1:15–21.) The pore size of Gynemesh PS is approximately 2,500 µm, and thus allows for excellent tissue integration and the passing of leukocytes and macrophages to clear any pathogens.

Prior to the commercial release of the Prolift device, Cosson and colleagues did a retrospective multi-center study of 687 patients treated with the Prolift mesh according to the protocol described by the TVM group surgeons.[7] The authors found intra-operative complications to be rare, occurring in only 1.32% of cases. They also found that short-term post-operative complications were uncommon, only occurring in 2.49% of patients. Only 1.32% of the patients experiencing post-operative complications required surgical treatment, and most of them were benign (1.75% hematomas and 0.29% perineal abscess). More serious complications like perineal cellulitis, vesico-vaginal or rectovaginal fistulas occurred in only 0.15% of cases each. Vaginal erosion or granuloma formation requiring surgical treatment occurred in 6.7% of patients. De novo stress incontinence occurred in 5.4% of the patients studied. The authors noted a 94.7% cure rate. Based on the study, the authors concluded that the technique was safe in the short-term, and that "Prolift mesh is obviously an interesting improvement in organ prolapse surgery."

c. The Safety and Efficacy of Gynemesh PS and the Prolift Device

Review of scientific reports of the use of Gynemesh and pelvic reconstructive surgery date back to 2001. De Tayrac described 36 patients undergoing cystocele repair using Gynemesh

[7] Cosson M, et al., Prolift Mesh (Gynecare) for Pelvic Organ Prolapse Surgical Treatment Using the TVM Group Technique: A Retrospective Study of 687 Patients. ICS 2005 Abs. 121.

with 13 month follow-up and 100% success with one mesh excision under local anesthesia for non-symptomatic exposure.[8]

Several studies demonstrate the versatility of Gynemesh PS, describing its use in various gynecologic procedures other than transvaginal procedures. Weiden described up to four-year follow-up of abdominal colposacropexy and hysterosacropexy using Gynemesh with bone anchoring and reported excellent anatomical results and low complication rates. This study is indicative of the many different uses to which the product can be put.[9] Agarwala describes in 2007 the use of Gynemesh for laparoscopic sacral colpopexy for recurrent prolapse of the apex or severe uterine prolapse. 74 patients were treated with Gynemesh. Subjective and objective cure was 97 and 100%, respectively. There were no cases of graft exposure or recurrence with a median follow-up of 24 months.[10]

Lucente in 2004 described 160 patients undergoing vaginal or abdominal/vaginal repair with a less than 10% exposure rate and success of 76% in reducing the prolapse to stage 0-1. The authors concluded that POP repair using GYNEMESH PS "is safe, with a low rate of significant mesh-related complications."[11] In 2006, Ali and colleagues described 108 patients undergoing anterior colporrhaphy with Gynemesh PS augmentation. They encountered no intra-operative complications, a 6.6% recurrence rate, and a 6.5% exposure rate.[12]

Collinet and colleagues described in 2006 the management of transvaginal mesh techniques for repair of pelvic prolapse using a vaginal approach and the use of Gynemesh. In the paper, it is described that the ideal mesh for pelvic reconstructive repair is monofilament polypropylene with large pores. The study was a continuous retrospective trial of more than two years, and was designed to identify the risk factors for exposure of mesh material and management strategies for postoperative complications. 277 patients undergoing surgery for pelvic prolapse using the TVM technique—using risk factors of body mass index, age, menopausal status, hormonal replacement therapy, previous surgical repair and hysterectomy—were included. Mesh exposure was less than 1% when the uterus was preserved. Management of mesh exposure involved local treatment combined with partial resection of the mesh if the local treatment proved inadequate. The local treatment was further enhanced with estrogen therapy.[13]

Deffieux described in 2006 management of 34 consecutive cases of vaginal mesh erosion following transvaginal repair of cystocele using Gynemesh or Gynemesh-Soft. 68% underwent local therapy using an estrogen cream. In 22% of cases, the mesh erosion had completely

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[8] De Tayrac R, et al., Cystocele Repair with a Fixation-Free Prosthetic Polypropylene Mesh. Abs. 2001.
[9] Van der Weiden RMF, et al., Colposacropexy With Mesh or Collagen Implant and Titanium Bone Anchors Placed in Sacral Segments 3 and 4. J Pelvic Med & Surg 2003;9(1):9–14.
[10] Agarwala N, et al., Laparoscopic sacral colpopexy with Gynemesh as graft material—Experience and results. J Minimally Invasive Gynecol 2007;14:577–83.
[11] Lucente V, et al., A Clinical Assessment of GYNEMESH PS for the Repair of Pelvic Organ Prolapse. AUGS, SGS Oral Poster 55
[12] Ali S, et al., A Prospective Randomized Trial Using Gynemesh PS for the Repair of Anterior Vaginal Wall Prolapse. Int Urogynecol J 2006;17(Supp. 2):S171–S359 (Abs. 292).
[13] Collinet P, et al., Transvaginal mesh technique for pelvic organ prolapse repair: mesh exposure management and risk factors. Int Urogynecol J 2006;17:315–20.

disappeared with a follow-up of 2-9 months. 59% of the symptomatic patients required partial or complete excision of the mesh with vaginal closure under general anesthesia. The surgery ranged from 15-40 minutes in duration and was successful 77% of the time. 11% of the patients undergoing a primary repair required a second operation because of recurrence. The incidence of the de novo dyspareunia was 12% with vaginal mesh exposure and 11% in those who had no exposure post operatively.[14]

Sola in a 2006 report describes 42 mesh procedures using Gynemesh PS mesh for both cystocele and rectocele, having no postoperative complications and a 95% success for cystocele and 100% success for rectocele repair.[15]

Hoenil Jo in 2007 evaluated 26 patients with stage III or IV pelvic organ prolapse for 2 years after Gynemesh vaginal repair. Success was 94% objective cure with no tissue erosion or infections noted.[16]

Takeyama described in 2007 a modification of the Prolift procedure using Gynemesh PS. They implanted Gynemesh PS in 245 patients with pelvic organ prolapse and had no serious complications and a low recurrence and exposure rate (0.8 and 1.6%, respectively).[17] Al-Nazer and colleagues reported in 2007 the results of their study of 40 patients undergoing either anterior colporrhaphy or implantation of Prolene Soft mesh. They found both groups had improvement in their prolapse, urinary, and sexual symptoms, but the improvement was more significant in the Prolene Soft group. 95% of the Prolene Soft patients were cured, while 70% of the anterior colporrhaphy patients were cured. They also found that operative morbidity was generally lower in the Prolene Soft group.[18]

Caquant and Cosson in 2008 reported on a study of 684 patients undergoing the TVM procedure using Gynemesh PS performed between 2002-2004. The mesh exposure rate without concurrent hysterectomy was 4.7% and medical management was successful in 42% of cases. The study was limited by short-term follow up.[19] In 2008, Letouzey and colleagues reported the results of their study of 63 women undergoing cystocele repair using Gynemesh PS between 1999-2001. The patients were followed for five years, and the authors observed an 80%

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[14] Deffieux X, et al., Vaginal mesh extrusion after transvaginal repair of cystocele using a prosthetic mesh: Treatment and functional outcomes. J Gynecol Obstet Biol Reprod (Paris) 2006 Nov;35(7):678–84.

[15] Sola V, et al., Tension Free Monofilament Macropore Polypropylene Mesh (Gynemesh PS) in Female Genital Prolapse Repair. Int Braz J Urol 2006;32(4):410–15.

[16] Jo H, et al., Efficacy and outcome of anterior vaginal wall repair using polypropylene mesh (Gynemesh). J Obstet Gynecol Res 2007 Oct;33(5):700–04.

[17] Takeyama M, et al., Feasibility of the Tension-Free Vaginal Mesh Procedure Using Soft Polypropylene Mesh (Gyunemesh PS) in Japan. Int Urogynecol J 2007;18(Supp. 1):S25–S105 (Abs. 079).

[18] Al-Nazer MA, et al., Comparative Study Between Anterior Colporrhaphy Versus Vaginal Wall Repair with Mesh for Management of Anterior Vaginal Wall Prolapse. Int Urogynecol J 2007;18 (Suppl. 1):S25–S105 (Abs. 084).

[19] Caquant F, et al., Safety of Trans Vaginal Mesh procedure: Retrospective study of 684 patients. J Obstet Gynaecol Res 2008 Aug;34(4):449–56.

anatomic cure rate with an additional 20% improved. The vaginal exposure rate was 16% and no patient required reoperation for recurrent prolapse.[20]

In 2009, Natale and colleagues reported the results of an RCT studying Gynemesh PS and Pelvicol with two years of follow-up. They observed a 6.3% erosion rate in the Gynemesh PS patients, and four of the six of those patients underwent a concomitant hysterectomy. The cure rate for the Gynemesh PS cohort was 71.9%. Pre-operative pain was reported by 14 patients in the Gynemesh PS group and that dropped to 0 patients after surgery. Pre-operative dyspareunia was reported by 20 patients in the Gynemesh PS group, and that number dropped to 10 patients after surgery.[21]

Miller and colleagues, in 2011, reported the five-year results of 85 patients undergoing Gynemesh PS anterior and posterior repair with and without hysterectomy. The success rate in the treated compartment at five years was 77%, and the rate of mesh exposure was 19%. Before surgery, 21 patients reported unprovoked vaginal pain, 23 reported pain on examination, 15 had cystalgia, 24 had pain during Valsalva, and 46 had pain with prolonged standing. By five years, only one patient reported pain, which occurred on examination only. At five years, only one case of de novo dyspareunia was observed in those patients who were sexually active before surgery, while resolution of dyspareunia occurred in at least eight of twelve patients with pre-existing dyspareunia. The authors concluded that the TVM procedure remains stable over time when measuring both quality of life and vaginal prolapse symptom scores.[22] Young-Suk Lee and colleagues in 2010 reported on their study of the treatment of 49 women undergoing transvaginal repair of pelvic organ prolapse with Gynemesh PS. They noted a 71.4% cure rate and an improvement rate of 18.4%. They observed only one vaginal erosion at the 12-month follow-up, which was asymptomatic. The authors concluded that "[t]rans-vaginal repair of an anterior vaginal wall prolapse with the monofilament polypropylene mesh Gynemesh™ PS is an effective and safe procedure."[23] Cuevas et al. reported in 2011 on a study involving the use of Gynemesh PS to create a Prolift-like device for treatment of severe pelvic organ prolapse. They observed a low recurrence rate, low rates of intraoperative and perioperative complications, and a low rate of mesh erosion. The study population was 100% satisfied with surgery, and 89.5% found the surgery improved their quality of life.[24]

Farthmann and colleagues studied 200 patients receiving either non-absorbable polypropylene mesh or a partially absorbable polypropylene mesh for cystocele treatment over

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[20] Letouzey V, et al., Long-Term Results after Trans-Vaginal Cystocele Repair Using a Tension-Free Polypropylene Mesh. J Minimally Invasive Gynecol 2008;15:S1–S159 (Abs. 102).
[21] Natale F, et al., A prospective, randomized, controlled study comparing Gynemesh®, a synthetic mesh, and Pelvicol®, a biologic graft, in the surgical treatment of recurrent cystocele. Int Urogynecol J 2009;20:75–81.
[22] Miller D, et al., Prospective Clinical Assessment of the Transvaginal Mesh Technique for Treatment of Pelvic Organ Prolapse—5 Year Results. Female Pelvic Med & Reconstr Surg 2011 May/Jun;17(3):139–43.
[23] Lee YS, et al., Efficacy and Safety of "Tension-Free" Placement of Gynemesh PS for the Treatment of Anterior Vaginal Wall Prolapse. INJ 2010;14:34–42.
[24] Cuevas R, et al., Prolift Like (PL) Surgery: A Management Option for Severe Pelvic Organ Prolapse (POP) in a Public Hospital in a Developing Country. Int Urogynecol J 2011;22 (Suppl. 2):S197–S1766 (Abs. 1108).

three years. Consideration of mesh weight and foreign material were correlated with 200 patients randomized to conventional or a partially absorbable mesh. Management of mesh exposure, satisfaction with surgery, and postoperative pain were evaluated. Rate of mesh exposure was smaller in the partially absorbable mesh at 3.4% vs 7.5% at 36 months, but the authors found the rate of exposure to be low in both groups. Of the 200 patients, 27 patients had exposure of mesh, with 11 requiring surgical intervention. The rate of recurrent vaginal prolapse was higher in the partially absorbed mesh group. The mesh weight in the nonabsorbable group was 29 g/m^2 with porosity >75 µm. Interestingly, exposure rates varied from 0 to 20.4% between hospital groups, indicating that surgical technique is an important outcome-determining factor. Statistically significant risk factors for exposure uncovered were concomitant hysterectomy, smoking, cesarean section, and a longer incision. The authors concluded that use of synthetic mesh was a safe technique for treatment of pelvic prolapse. Patient satisfaction rates did not vary between the two groups.[25]

Samour and colleagues, in 2014, described the safety and efficacy of using Gynemesh PS for cystocele repair using a minimally invasive technique of transvaginal corkscrew application through the obturator foramen. 152 patients who underwent repair for cystocele grade 2 or greater using Gynemesh PS were followed for up to 36 months with a variable degree of dyspareunia observed in the first 3 months and marked improvement and even disappearance of pain for 90% of patients by the end of 6 months. 3% had persistent dyspareunia by the conclusion of the study. The rate of mesh exposure was 3.3%, reportedly due to the avoidance of excising vaginal epithelium and full-thickness dissection with lack of tension on the mesh. The authors concluded that transobturator placement of Gynemesh PS can be considered a minimally invasive and promising method for correction of cystocele and stress incontinence based on low rate of complications, high rate of success, and low incidence of recurrence.[26]

Dr. Marcus Carey and colleagues, in 2009, reported the results of a randomized controlled trial comparing anterior and posterior vaginal repair with Gynemesh PS augmentation or traditional anterior and posterior colporrhaphy. The success rate in the mesh group at one year post-op was 81%, but only 65% in the traditional anterior and colporrhaphy group. Patients had a high level of satisfaction with the surgery and both groups showed improvements in symptoms and quality-of-life data. New-onset dyspareunia was reported in 16% of sexually active women in the mesh group versus 15% in the non-mesh group.[27]

In 2006, Boulanger and colleagues published the results of a study in which they placed five different meshes—Vicryl, Vypro, Prolene, Prolene Soft, and Mersilene in the peritoneum of pigs to study the tissue integration and tolerance of the meshes. The authors found that the absorbable prostheses made of Vicryl and the non-absorbable prostheses made of polypropylene (i.e., Prolene and Prolene Soft) induced the least severe inflammatory reactions and produced the

[25] Farthmann J, et al., Lower exposure rates of partially absorbable mesh compared to nonabsorbable mesh for cystocele treatment: 3-year follow-up of a prospective randomized trial. Int Urogynecol J 2013;24:749–58.
[26] Samour H, et al., Minimally invasive cystocele repair technique using a polypropylene mesh introduced with the transobturator route. Arch Gynecol Obstet 2015 Jan;291(1):79–84.
[27] Carey M, et al., Vaginal repair with mesh versus colporrhaphy for prolapse: a randomised controlled trial. Br J Obstet Gynecol 2009 Sep;116(10):1380–1386.

best tissue integration. They concluded that Type I Amid monofilament material, such as polypropylene, seemed to be the best integrated and tolerated.[28] Memon developed a biomechanical test to evaluate mesh-reinforced repair as compared to suture-reinforced repair in an animal model. The conclusion of the study was that Gynemesh PS was the least likely synthetic material to fail after repeated cycles of stressing, and was superior to xenograft-reinforced repair and to suture-only repair.[29] In an animal study published in 2007, Bhende and colleagues studied Prolene Soft and other synthetic meshes, as well as naturally derived meshes, to observe the extent to which the meshes served "as a nidus for microbial attachment and growth, thus exacerbating surgical site infection." They found that "[t]he synthetic meshes did not potentiate infection . . . whereas the naturally-derived meshes did."[30]

A 2013 study looked at how pelvic organ prolapse affects sexual function and found that the use of mesh in anterior compartment repair was not associated with a worsening in sexual function or an increase in de novo dyspareunia when compared to traditional anterior colporrhaphy. It also noted that up to 64% of sexually active women attending a urogynecology clinic suffer from female sexual dysfunction.[31] Lowman and colleagues have reported that pelvic organ prolapse repair appears to have a high rate of associated dyspareunia regardless of whether the surgery is performed transvaginally or transabdominally. They also noted that baseline rates of dyspareunia range between 8–43% in women with pelvic organ prolapse, and that this fact makes the evaluation of de novo dyspareunia following prolapse repair quite difficult.[32]

Ongoing technological advances of synthetic meshes using polypropylene have been a moving target, with development of lighter and less stiff materials over the last 10 years. At the time of introduction of Gynemesh PS in the early 2000s, the material was considered the least stiff and most porous mesh to receive FDA clearance and introduction into the surgical market. The stiffness, weight, and porosity of Gynemesh PS has subsequently moved to the middle of the spectrum of synthetic mesh products as recent science has favored the least stiff, lightest weight, and most porous material possible. Nonetheless, Gynemesh PS is still a lightweight, large-pore mesh. There is a point of diminishing returns, as some of the lightest weight meshes have the most deformation and can fail in the physiologic environment of the vagina. Complications that are described are more related to surgical technique and patient selection than the individual mesh product used. The avoidance of large and "T" incisions, concomitant hysterectomy, tobacco use, obesity, exposure to radiation therapy for pelvic cancer, chronic use of steroids, and advanced age all play a significant role in the incidence of vaginal mesh exposure. Injury to either bladder intestine or rectum is a direct result of surgical misadventure. Patients with

[28] Boulanger L, et al., Tissue integration and tolerance to meshes used in gynecologic surgery: An experimental study. Eur J Obstet & Gynecol and Reprod Biol 2006;125:103–08.
[29] Memon HU, et al., Comparison of graft-reinforced repairs and suture repair using a novel biomechanical test
[30] Bhende S, et al., Infection Potentiation Study of Synthetic and Naturally Derived Surgical Mesh in Mice. Surg Infections 2007;8(3):405–14.
[31] Dietz V and Maher C, Pelvic organ prolapse and sexual function. Int Urogynecol J 2013;24:1853–1857.
[32] Lowman JK, et al., Does the Prolift system cause dyspareunia? Am J Obstet Gynecol 2008 Dec;199:707.e1–707.e6.

symptomatic and increasing vaginal prolapse who have failed previous native suture plication often require augmented repairs with xenograft or synthetic materials.

The Prolift device was the most studied mesh kit for pelvic organ prolapse treatment and the studies showed high success rates with minimal complications.[33] Van Raalte in 2007 studied 350 patients undergoing the Prolift procedure with median follow-up of 6 months, and observed a mesh exposure rate of 1.1%, with all treated with office resection and/or vaginal estrogen. The postoperative pop-Q cure rate was 90.6% with a dyspareunia rate of 6.3%. One patient required in office vaginal injection for pain treatment and 1 patient had a surgical mesh resection.[34]

Withagen and colleagues, in 2011, published the results of a randomized controlled trial comparing 97 women undergoing conventional repair and 93 women undergoing Prolift repair. One year after surgery, they found anatomic failure of the procedure in 45.2% of the patients undergoing a conventional repair and in 9.6% of the Prolift patients ($p < .001$; OR 7.7; 95% CI 3.3-18). Fourteen of the Prolift patients (16.9%) had a mesh exposure, but nine of the fourteen were asymptomatic and treated with local estrogen only. Five underwent an additional outpatient surgery to excise the exposed mesh. Those exposures resolved. In both groups, dyspareunia decreased at twelve months compared to baseline, and there was no statistically significant difference between the two groups. There was no statistically significant difference in de novo dyspareunia between the two groups at twelve months.[35]

In 2011, Altman and colleagues published in the New England Journal of Medicine their multi-center RCT comparing anterior colporrhaphy and Prolift surgery for the treatment of cystocele. They found that the primary endpoint of success (POP-Q stage 0 or 1) was significantly more common in the Prolift group (60.8%) than it was in the colporrhaphy group (34.5%). The rate of intra-operative hemorrhage was higher in the Prolift group. Re-operation to correct mesh exposure during the one-year follow-up period occurred in only 3.2% of the 186 patients in the Prolift group. Dyspareunia was higher in the Prolift group, but the difference was

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[33] Halaska M, et al., A multicenter, randomized, prospective, controlled study comparing sacrospinous fixation and transvaginal mesh in the treatment of posthysterectomy vaginal vault prolapse. Am J Obstet Gynecol 2012;207:301.e1–7; da Silveira S, et al., Multicenter, randomized trial comparing native vaginal tissue repair and synthetic mesh repair for genital prolapse surgical treatment. Int Urogynecol J 2015 Mar;26(3):335–342; Svabik K, et al., Comparison of vaginal mesh repair with sacrospinous vaginal colpopexy in the management of vaginal vault prolapse after hysterectomy in patients with levator ani avulsion: a randomized controlled trial. Ultrasound Obstet Gynecol 2014 Apr;43(4):365–371; de Landsheere L, et al., Surgical intervention after transvaginal Prolift mesh repair: retrospective single-center study including 524 patients with 3 years' median follow-up. Am J Obstet Gynecol 2012 Jan;206(1):83.e1–7; Withagen MI, et al., Trocar-Guided Mesh Compared With Conventional Vaginal Repair in Recurrent Prolapse: A Randomized Controlled Trial. Obstet Gynecol 2011 Feb;117(2):242–250; Sokol AI, et al., One-year objective and functional outcomes of a randomized clinical trial of vaginal mesh for prolapse. Am J Obstet Gynecol 2012 Jan;86:e1–e9; Altman D, et al., Anterior Colporrhaphy versus Transvaginal Mesh for Pelvic-Organ Prolapse. N Engl J Med 2011;364:1826–1836.

[34] van Raalte H, et al., Short-Term Results of the Prolift Procedure in 350 Patients Used in the Treatment of Pelvic Organ Prolapse. Int Urogynecol J 2007;18 (Suppl. 1):S25–S105 (Abs. 083).

[35] Withagen MI, et al., Trocar-Guided Mesh Compared With Conventional Vaginal Repair in Recurrent Prolapse. Obstet Gynecol 2011 Feb;117(2 Pt 1):242–50.

not statistically significant. There was no statistically significant difference in pelvic or genital pain between the two groups.[36]

Halaska and colleagues published the results of their randomized controlled trial involving 168 patients receiving either a Prolift or SSLF with one-year follow-up. Prolapse recurred after 12 months in 39.4% of the SSLF patients and 16.9% of the Prolift patients ($p = 0.003$). Mesh exposures occurred in 20.8% of the Prolift patients, but only 25% of those were symptomatic. Six of the symptomatic erosions resolved with local estrogen therapy and ten were surgically treated—six under general anesthesia and four under local anesthesia, but all successfully treated. Overall, only 7.6% of all the mesh patients required resection under general anesthesia.[37]

Sokol and colleagues in 2012 reported on the results of their one-year randomized controlled trial comparing treatment of women with women with stage ≥ 2 prolapse with either traditional repair or Prolift. They found that both operations resulted in objective and subjective improvement of prolapse, but the mesh resulted in a higher reoperation rate. They saw a 15.6% mesh exposure rate and a 9.3% reoperation rate for exposure in the Prolift group. All of the exposures resolved after outpatient trimming without further exposures. In the traditional repair patients, 15% had apical Gore-Tex suture exposures. Despite the 15.5% exposure rate in the Prolift patients, both groups had high subjective satisfaction at one year, and there was no significant difference found between the groups with respect to sexual function at one year.[38]

In 2014, Svabik and colleagues published a study comparing Prolift surgery to sacrospinous ligament fixation surgery in patients who had had a hysterectomy and a levator ani avulsion injury. At one-year follow-up, they saw a 3% rate of anatomical failure in the patients who received Prolift repair, and a 65% frate of anatomical failure in the SSLF group. There were no major complications such as heavy bleeding, bladder injury, or bowel injury in either group. There were three mesh exposures in the Prolift group at the three-month follow-up but no additional exposures at the one-year follow-up. One of those three was asymptomatic and treated conservatively. Re-operation for stress urinary incontinence was significantly higher in the Prolift group, but the authors theorized that the lower rate in the SSLF group may have resulted from a higher incidence of urethral king in the SSLF group, which masked stress incontinence in those with recurrent cystocele. Dyspareunia rates were low, with two patients experiencing it in the Prolift group and one in the SSLF group.[39]

In 2015, da Silveira and colleagues published the results of their multi-center randomized trial comparing native tissue repairs with Prolift. The authors found that complications were

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[36] Altman D, et al., Anterior Colporrhaphy versus Transvaginal Mesh for Pelvic-Organ Prolapse. N Engl J Med 2011 May;364(19);1826–36.

[37] Halaska M, et al., A multicenter, randomized, prospective, controlled study comparing sacrospinous fixation and transvaginal mesh in the treatment of posthysterectomy vaginal vault prolapse. Am J Obstet Gynecol 2012 Oct;207:301.e1–7.

[38] Sokol AI, et al., One-year objective and functional outcomes of a randomized clinical trial of vaginal mesh for prolapse. Am J Obstet Gynecol 2012 Jan;206:86.e1–9.

[39] Svabik K, et al., Comparison of vaginal mesh repair with sacrospinous vaginal colpopexy in the management of vaginal vault prolapse after hysterectomy in patients with levator ani avulsion: a randomized controlled trial. Ultrasound Obstet Gynecol 2014 Apr;43(4):365–71.

statistically significantly higher in the mesh group, but the "only between-group difference was related to mesh exposure, which occurred in 20% of the patients in the mesh group. Of those patients, however, only three patients required revisions surgery; in the other fifteen patients the exposure was treated with topical estrogen. The numbers of patients with dyspareunia, pain, and recurrence of prolapse were higher in the native tissue cohort, but the differences were not statistically significant. Quality of life scores were significantly improved in each group, but there was a greater improvement of quality of life in the mesh group despite the increased rate of exposures. Anatomical efficacy was higher in the mesh group in the anterior compartment.[40]

Benbouzid and colleagues did a study of Prolift patients with 4.5-year follow-up. They observed an 85.3% cure rate (defined as POP-Q stage 0–1) with no recurrence. Mesh exposure only occurred in 4 of the 75 patients (5.3%); two of whom were treated with topical estrogen, and two who underwent revision. There were no recurrences beyond POP-Q Stage II.[41]

De Landsheere and colleagues conducted a retrospective single-center study of 524 patients undergoing Prolift, with a median follow-up of three years. The global reoperation rate was 11.6%. They found the rate of mesh complications was low.[42]

Maher and colleagues more recently analyzed 37 randomized controlled trials involving 4,023 women comparing different types of vaginal repair (mesh, biologic graft, or native tissue) and their analysis was recently published by The Cochrane Collaboration. While they found more women in the mesh group needed reoperation for the combined outcome of prolapse, SUI, or mesh exposure, rates of repeat surgery for prolapse were lower in the mesh group, and there was no evidence of a difference between the mesh and other groups in rates of repeat incontinence surgery. Eight percent of the mesh patients needed reoperation for mesh exposure. Recurrent prolapse was less likely in the mesh patients than in the other patients. The authors found no evidence of a difference in dyspareunia rates between the groups, and the mesh patients awareness of prolapse at 1–3 years was less likely than for the patients in the other groups.[43]

I have personally performed over 1,000 procedures involving implantation of Prolene polypropylene mesh for treatment of stress urinary incontinence or pelvic organ prolapse, and have found the Prolene polypropylene products to be safe and efficacious when following the appropriate patient selection and the technique described by the product instructions for use and sound medical judgment and surgical technique and concepts. I have lectured and proctored physicians on the safe use of Prolene polypropylene devices for pelvic floor surgery since 2000. The devices are high quality, straightforward, and the polypropylene mesh is stable over time, as I have patients implanted 15 years ago and see no long-term complication trends. Since the television advertisements claiming pelvic mesh is a dangerous product, I have received hundreds

[40] Da Silveira, et al., Multicenter, randomized trial comparing native vaginal tissue repair and synthetic mesh repair for genital prolapse surgical treatment. Int Urogynecol J 2015 Mar;26(3):335-42.
[41] Benbouzid S, et al., Pelvic organ prolapse transvaginal repair by the Prolift system: Evaluation of efficacy and complications after a 4.5 years follow up. Int J Urol 2012;19:1010–1016.
[42] de Landsheere L, et al., Surgical intervention after transvaginal Prolift mesh repair: retrospective single-center study including 524 patients with 3 years' median follow-up. Am J Obstet Gynecol 2012 Jan;206(1):83.e1–7.
[43] Maher C, et al., Transvaginal mesh or grafts compared with native tissue repair for vaginal prolapse. Cochrane Database Syst Rev. 2016 Feb 9;2:CD012079.

of phone calls from anxious patients with fears of product recalls and future complications. The overwhelming majority of those anxious patients have excellent outcomes and no adverse symptoms. The effect on current patients is to create fear that a synthetic sling will cause future problems and many choose not to proceed to treatment. There is a 30% reduction in the number of patients undergoing stress incontinence and pelvic reconstructive surgery.[44]

As set forth above, the efficacy and safety of the Ethicon's Gynemesh PS and Prolift is well-reported. The peer-reviewed, published clinical data shows that procedures involving Gynemesh PS and the Prolift device can be performed safely and effectively. The studies show that most patients do not experience dyspareunia or pelvic pain after undergoing transvaginal mesh repair for pelvic organ prolapse.

Additionally, the professional organizations AUGS and SUFU—non-profit organizations representing over 2,000 practicing physicians, nurse practitioners, physical therapists, nurses, health care professionals and researchers dedicated to treating female pelvic floor disorders—have made the following statements regarding the safe use of polypropylene and the benefits of providing surgeons with options for treating pelvic floor disorders:

Polypropylene material is safe and effective as a surgical implant. Polypropylene has been used in most surgical specialties (including general surgery, cardiovascular surgery, transplant surgery, ophthalmology, otolaryngology, gynecology, and urology) for over five decades, in millions of patients in the US and the world (personal communication with manufacturers of polypropylene suture and mesh). As an isolated thread, polypropylene is a widely used and durable suture material employed in a broad range of sizes and applications. As a knitted material, polypropylene mesh is the consensus graft material for augmenting hernia repairs in a number of areas in the human body and has significantly and favorably impacted the field of hernia surgery. As a knitted implant for the surgical treatment of SUI, macroporous, monofilament, light weight polypropylene has demonstrated long term durability, safety, and efficacy up to 17 years.[45]

* * * *

> The American Urogynecologic Society strongly opposes any restrictions by state or local medical organizations, healthcare systems, or insurance companies which ban currently available surgical options performed by qualified and credentialed surgeons on appropriately informed patients with pelvic floor disorders.[46]

I agree with these position statements.

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[44] Perkins CE, Warrior K, Eilber KS, et al. The Role of Mid-urethral Slings in 2014: Analysis of the Impact of Litigation on Practice. Curr Bladder Dysfunct Rep (2015) 10:39-45. DOI 10.1007/s11884-014-0278-z; Koo K, Gormley EA, Abstract MP81-05: Transvaginal Mesh in the Media Following the 2011 FDA Update.

[45] AUGS-SUFU, Position Statement on Mesh Midurethral Slings for Stress Urinary Incontinence (Jan. 3, 2014).

[46] AUGS Position Statement on Restriction of Surgical Options for Pelvic Floor Disorders (2013).

Plaintiffs' experts' theory of mesh degradation is not substantiated in the literature or in my personal experience using polypropylene slings and mesh for incontinence treatment and pelvic reconstruction. Studies of explanted mesh are difficult to interpret, as there is damage to the material during explantation, treatment with chemicals to remove the collagen and biologic matrix that has incorporated into the mesh, and preparation onto slides for microscopic examination. There is no literature to support clinically significant mesh degradation in humans. Polypropylene suture is used by vascular surgeons on major blood vessels and in my practice when tying off renal arteries and repairing the largest vein in the body; the vena cava. If there was a question of degradation or loss of strength over time, Prolene suture would not be the suture of choice for the highest-risk surgery. The studies often relied on by plaintiffs' experts offering the opinion that the Prolene mesh degrades are unreliable and do not support that theory. For instance, the Clavé study from 2010 is unreliable and does not show degradation. The chemical analyses performed on a limited subset of the specimens does not show degradation, and the scanning electron microscope photos in the study show surface cracking that could be from biologic material and handling or preservation rather than the cracking of the polypropylene itself. Also, the sample analyzed in the study was only 32 out of the 100 specimens, and the authors fail to discuss how those 32 specimens were selected. They also fail to discuss whether the mesh was damaged during surgical explantation.

Nor have I seen a problem with shrinking, contraction or pore collapse when placed according to the IFU. Scar tissue that forms after any pelvic surgery contracts, and tissue incorporating into implanted mesh is no exception, but the mesh itself does not contract.

Some plaintiffs' experts' have said that placement of transvaginal mesh is dangerous and violates one of the most basic tenets of surgical teachings in that it involves placing a permanent implant into a human through a contaminated surgical field . If that theory was correct, the majority of patients receiving transvaginal mesh would have infections. However, vaginal infections following implantation of transvaginal mesh are very rare. Such opinions by plaintiffs' experts are not borne out in facts. There are tens of thousands of women with transvaginally placed mesh who are doing well, including in my own practice in the past fifteen years. If what plaintiffs' experts are saying was true, the majority of patients would have complications rather than a small percentage. Operative prep of the vagina is performed prior to the surgery, which maximizes sterility. The available medical literature does not indicate an increased risk of infection with transvaginal mesh procedures like the Prolift.

Plaintiffs' experts contend that the Prolift is defective and/or dangerous because it involves "blind" passage of the graft. However, many pelvic floor surgical procedures are performed with tactile palpation based on a knowledge of relevant anatomy, and the Prolift is no different in that regard. Injury to adjacent organs and vessels is a risk of all prolapse surgeries, not just those involving mesh grafts placed transvaginally.

There is no practical or clinical difference between mechanically cut or laser-cut mesh in terms of how it is deployed or incorporated in the tissues.[47] Mesh is not pre-stretched to 50%

[47] ETH.MESH.01784823-28 (CER Laser Cut Mesh); ETH.MESH.01222075-79 (Elongation Characteristics of Laser Cut Prolene Mesh for TVT); ETH.MESH.06696367-79 (Performance Evaluation

elongation before it is used. The mesh must have porosity large enough to encourage fibroblast and collagen deposition for incorporation, and it must have enough elasticity to allow give during dynamic stressing that occurs with activity. Mesh requires an optimal level of stiffness to properly do its job. Both laser-cut and mechanically cut Prolene mesh is safe and efficacious as demonstrated by the medical literature and in my experience.

Plaintiffs' experts have also claimed that the Gynemesh PS mesh in the Prolift is cytotoxic and causes an excessive inflammatory response. This is not supported in the literature, and I have not seen it in my practice. The mere presence of chronic inflammatory cells in a tissue specimen does not prove that there is a chronic inflammatory process that is active. Such cells can be present but quiescent, and can be seen in vaginal tissue even when no mesh or other foreign body has been implanted.

Plaintiffs' experts may claim that Ultrapro or Vypro mesh would have been a safer alternative to the Prolene Soft mesh. However, with respect to Vypro, a study of the use of that mesh in pelvic floor surgery showed that tolerance of the Vypro mesh was "very poor" and associated with high rates of erosion and cicatrisation.[48] With respect to Ultrapro, the study often cited by plaintiffs' experts in support of that material as a safer alternative to the Prolene TVT mesh is the Okulu study, but that study shows the same number of erosions (2) occurred in both the Prolene Soft cohort and the Vypro cohort, despite Vypro's larger pore size and lighter weight, and that the Ultrapro group just had one fewer erosion.[49]

Plaintiffs' experts sometimes suggest or claim that mesh made of Prolene polypropylene is carcinogenic, but there is no reliable scientific evidence to support the theory or claim that polypropylene can cause cancer or sarcoma. In the more than 1,000 cases in which I have implanted one of the Ethicon Prolene polypropylene products, I have not seen a single case of cancer attributable to the mesh. The literature also refutes plaintiffs' experts' suggestion or claim.[50] (King AB, et al. Is there an association between polypropylene midurethral slings and malignancy? Urology. 2014 Oct;84(4):789-92; King AB, Goldman HB. Current controversies regarding oncologic risk associated with polypropylene midurethral slings. Curr Urol Rep. 2014 Nov;15(11):453; Linder BJ, et al., Evaluation of the local carcinogenic potential of mesh used in the treatment of female stress urinary incontinence. Int Urogynecol J 2016 DOI:10.1007/s00192-016-2961-4.) The medical literature contains no case reports of tumors caused by or associated with polypropylene implantation despite the fact that polypropylene has been implanted in

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of TVT U Prolene Mesh); Lin AT, et al., In Vivo tension Sustained by Fascial Sling in Pubovaginal Sling Surgery for Female Stress Urinary Incontinence, J Urol , 2005 Mar;173(3):894–897.

[48] Denis S, et al., Pelvic Organ Prolapse Treatment by the Vaginal Route Using a Vypro Composite Mesh: Preliminary Results About 106 Cases. ICS IUGA 2004; Abstract 620.

[49] Okulu E, et al., Use of three types of synthetic mesh material in sling surgery: A prospective randomized clinical trial evaluating effectiveness and complications. Sand J Urol 2013;47:217–224.

[50] King AB, et al. Is there an association between polypropylene midurethral slings and malignancy? Urology. 2014 Oct;84(4):789-92; Moalli P, et al., Polypropylene mesh: evidence for lack of carcinogenicity. Int Urogynecol J 2014, DOI 10.1007/s00192-014-2343-8; King AB, Goldman HB. Current controversies regarding oncologic risk associated with polypropylene midurethral slings. Curr Urol Rep. 2014 Nov;15(11):453.

millions of people. (AUGS & SUFU, Frequently Asked Questions by Providers—Mid-urethral Slings for Stress Urinary Incontinence (available at http://www.augs.org/p/bl/et/blogaid=194).)

V. Prolift's Instructions for Use and Other Educational Materials

a. Ethicon's Instructions for Use, Surgical Technique Guide, and Surgeon's Resource Monograph

Each Prolift device was accompanied by an Instructions for Use (IFU) document. The IFU describes the Prolift Total, Anterior, and Posterior Pelvic Floor Repair Systems. It notes that the systems "are indicated for tissue reinforcement and long-lasting stabilization of fascial structures of the pelvic floor in vaginal wall prolapse where surgical treatment is intended, either as mechanical support or bridging material for the fascial defect." (ETH.MESH.02341522-89.) It contains a detailed description of the total, anterior, and posterior implants, and diagrams that demonstrate the general use of each device. The IFU starts with a request to the user to "Please read all information carefully," and then cautions that "[f]ailure to properly follow instructions may result in improper functioning of the devices and lead to injury." It also notes that "[t]raining on the use of the GYNECARE PROLIFT Pelvic Floor Repair Systems is recommended and available," and advises the user to contact his or her company sales representative to arrange for the training. The IFU also directs the surgeon to "[r]efer to the recommended surgical technique for the GYNECARE PROLIFT Pelvic Floor Repair Systems for further information on the GYNECARE PROLIFT procedures." It also provides instructions for the placement of sutures, staples, or other fixation devices (if used) at a certain distance away from the edge of the mesh The IFU sets forth the contraindications for using the product.

The IFU then sets forth Warnings and Precautions and potential Adverse Reactions. It cautions that "[u]sers should be familiar with surgical procedures and techniques involving pelvic floor repair and nonabsorbable meshes before employing the GYNECARE PROLIFT Pelvic Floor Repair Systems." It also notes that "[a]cceptable surgical practices should be followed in the presence of infected or contaminated wounds," and advises that after surgery, patients "should be advised to refrain from intercourse, heavy lifting and/or exercise (e.g. cycling, jogging) until the physician determines when it is suitable for the patient to return to her normal activities." The IFU warns the surgeon to "[a]void placing excessive tension on the mesh implant during handling." It also directs the surgeon to "[r]efer to the recommended surgical technique for the GYNECARE PROLIFT Pelvic Floor Repair System for further information on the GYNECARE PROLIFT procedures." The IFU warns the surgeon to use the Prolift "with care to avoid damage to vessels, nerves, bladder and bowel," and that "[a]ttention to patient anatomy and correct use of the device will minimize risks." It warns that "[t]ransient leg pain may occur and advises that it can usually be managed with mild analgesics. It also notes that the potential adverse reactions associated with the device "are those typically associated with surgically implantable materials, including infection potentiation, inflammation, adhesion formation, fistula formation, erosion, extrusion and scarring that results in implant contraction." Finally, it warns that "[p]unctures or lacerations of vessels, nerves, bladder, urethra or bowel may occur during GYNECARE PROLIFT Guide passage and may require surgical repair.

The IFU and the warnings contained therein are adequate and allow for the safe use of the device. The instructions are such that a trained and experienced physician could implant the mesh safely and effectively. The IFU is not intended to teach surgical technique, which is assumed to have been in the skill set of the surgeon. Every surgeon should be aware of the intraoperative and post-operative risks inherent in the use of surgical mesh. A surgeon need not be taught the entire practice of medicine in an IFU. The totality of surgical risks is not included in the IFU for surgeons. Surgeons have training from numerous sources—medical school, residency, maybe fellowships, colleagues' experiences, their own experience, literature, etc. The IFU is used by the surgeon to become familiar with the specific device, the handling, placement and deployment in the manner that maximizes safety and efficacy. The IFU is never assumed to be a completely comprehensive list of all the possible adverse complications that are low prevalence. The IFU is intended to guide the surgeon to perform the procedure as the device was designed.

Mesh exposure and erosion or extrusion are the only unique risks to mesh surgeries, and are essentially wound complications. Wound complications can also occur with other surgeries. Mesh exposure can be caused by poor quality tissue due to atrophic vaginitis, history of pelvic radiation therapy, too superficial dissection prior to sling placement, hematoma, tobacco usage, and early sexual activity.

The IFU lists indications for use, contraindications, most prevalent risks, and a detailed description of how to deploy the mesh safely. IFUs in general are not intended to list every possible adverse event or post-operative complication. The IFU is generally understood to be a guide in the proper deployment of the device. Surgeons are trained in residency how to manage vaginal surgery with anatomy, handling of tissues, defining surgical planes, and perioperative care. The IFU functions to describe how this particular device is best deployed but the patient selection, preoperative informed consent, perioperative management, and post-operative care of the patient is the surgeon's responsibility. The patient's degree of severity of vaginal prolapse, with consideration of patient age, tissue integrity, previous pelvic surgery, health status, tobacco usage, and steroid or opioid dependency leads the surgeon to make a complex decision about surgical approach and the likelihood of success.

Plaintiffs' experts may claim that pain, dyspareunia should have been warned about in the IFU. I disagree. Pelvic floor surgeons know that pain and dyspareunia may occur with any pelvic floor surgery, and they know that any surgical complications can be temporary or permanent. Surgeons know that surgical complications can be mild, moderate, or severe. Surgeons need not be specifically warned in an IFU of these fundamental surgical risks. Published data supports the fact that dyspareunia rates following pelvic floor surgery with Prolene Soft mesh are low.[51]

[51] Fatton B, et al., Transvaginal repair of genital prolapse: preliminary results of a new tension-free vaginal mesh (Prolift™ technique)—a case series multicentric study. Int Urogynecol J 2007;18:743–752 (noting that among the 30 patients known to be sexually active, 76.6% had resumed sexual intercourse at three months follow-up, while only three patients complained of dyspareunia); Paplomata E, et al., Genital Floor Repair Using Polypropylene Meshes: a Comparative Study. 2007 (Abs. 482) (noting that only two patients of 56 that underwent prolapse repair with Gynemesh or Prolift developed dyspareunia during 21-month follow-up); Jacquetin B, et al., Total transvaginal mesh (TVM) technique for treatment

Ethicon also produced a Surgical Technique Guide and a Surgeon's Resource Monograph. The Surgical Technique Guide provided detailed instructions on preparing the patient for Prolift surgery and the total, anterior, and posterior procedures performed in conjunction with vaginal hysterectomy. It noted that "[r]etrospective data analysis suggests that the rate of mesh exposure may be higher when performing the TVM procedure with and without concurrent hysterectomy, or where the patient had a prior hysterectomy (for the Prolift Total procedure)." The Surgeon's Resource Monograph was based in part on the experience of pelvic floor surgeons from around the world who had performed Prolift procedures in a large number of cases. The Monograph provided background information on the development of Prolift, and correctly noted that it contained "information that is not available on most procedures." It set forth expert opinions on the use of the Prolift Total, Anterior, and Posterior Pelvic Floor Repair System, and discussed patient selection and preparation, surgical technique, anesthesia and hydrodissection, incisions, additional sutures, mesh handling, and complications including hemorrhage, visceral injury, infection, erosion, exposure, extrusion, dyspareunia and vaginal pain. It also included a summary of the available clinical data. The instructions and warnings provided by Ethicon in these documents were adequate and helpful to surgeons.

Ethicon also provided a professional education program that supplemented the IFU. There was a preceptorship in which physicians would attend didactic lectures discussing patient selection, surgical technique, and literature on the device, followed by time in a cadaver lab spent learning how to implant the devices. Surgeons were also provided the opportunity to observe other surgeons implanting the devices in patients, or to have a surgeon experienced in using the device scrub in on a surgery to oversee the surgeon's implantation of the device. Complications and the management of complications were discussed in these professional education programs, which were extremely helpful. This professional education program did not, however, take the place of surgeon credentialing at the hospital level.

c. Prolift Brochures

Ethicon produced brochures regarding the Prolift device, which surgeons could provide to patients considering surgical treatment of their pelvic organ prolapse. The brochures background information regarding pelvic organ prolapse such as a general description of pelvic organ prolapse, the various symptoms one can experience with pelvic organ prolapse, the causes of the condition, and how common it is. The brochures also described the various types of pelvic organ prolapse and provided diagrams depicting the various types. The brochures discussed treatment options—both conservative and surgical—for pelvic organ prolapse, and noted that patients "should undergo a thorough evaluation to ensure a proper diagnosis" of pelvic organ prolapse. (ETH.MESH.03904968–75.) They described the Prolift device, how it is different from other surgical alternatives, and how the device works. They provide information on what the patient can expect during the procedure and after they go home, and they discussed risks of the Prolift procedure, including "injury to blood vessels of the pelvis, nerve damage, difficulty urinating, bladder and bowel injury," and exposure of the mesh into the vaginal canal. All of this information was set forth in terms that are understandable to those without any medical

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of pelvic organ prolapse: a 5-year prospective follow-up study. Int Urogynecol J 2013 Oct;24(10):1679–1686.

training. The brochures then set forth the indications, contraindications, warnings and precautions, and adverse reactions associated with the device.

The product brochures provided adequate information regarding the Prolift device and was helpful to patients in my practice. The brochures did not, however, serve as a substitute for a comprehensive informed consent discussion between the surgeon and the patient.

VI. The Design of Prolift

a. The Usefulness, Desirability, and Safety of the Prolift Device

Gynemesh PS mesh—the mesh used in the Prolift device—is very useful to surgeons because it is a lightweight, large-pore, knitted, monofilament Prolene polypropylene mesh that is well-tolerated by the body and adds needed reinforcement to native tissue for repair of fascial defects. The large pore-size of the mesh allows for tissue incorporation and the passage of macrophages and leukocytes to help clear any bacteria that could lead to an infection. Unlike allograft or xenograft material, synthetic mesh like Gynemesh PS is readily available, is not met with cultural or religious objections, and presents no risk of disease transmission by viruses, prions, and bacteria.

The polypropylene monofilament used to knit the mesh has been safely used in surgery as suture throughout the body for over 50 years, and has been shown to be stable and does not degrade in the body over time. The device is also useful because it comes with instructions for use, a tracking lot number for safety and batch analysis, as well as MDR reporting and FDA analyses. The mesh used in the device is not met with cultural or religious objections like allografts or xenografts, and is extremely effective and durable, with very low recurrence rates. As discussed in the studies above, there is an extensive body of literature supporting the safety of the mesh and the efficacy of treating pelvic organ prolapse with the device.

It is comforting as a surgeon to be using a product that is known to have the largest amount of peer-reviewed data from multiple institutions substantiating a safe, reliable, reproducible technique and material. Prolene has been around for 50 years, been safely used in various applications, and the body's reaction to the material is known.

Complications are usually surgery-related and not mesh-specific. Exposures are uncommon and manageable, occurring in a small minority of cases. The cause can be poor tissue integrity caused by estrogen deficiency, delayed wound healing due to diabetes, steroid usage, hematoma formation, or placing the sling too superficially. Treatment includes application of topical estrogen cream, re-closure of the mucosal edges, and limited mesh excision if necessary. The excision can be performed in an office setting under local anesthesia or under light sedation in an OR. Dyspareunia is rare following implantation of the device, and most sexual dysfunction occurring after pelvic organ prolapse surgery is connected to concomitant hysterectomy and/or oophorectomy. Graft-related complications can occur with any material used for augmentation, whether it is synthetic or biologic graft material or synthetic suture material. Abed and

colleagues' systematic review in 2011 showed that erosions happen in 10.1% of patients receiving biological grafts and in 10.3% of patients receiving synthetic grafts.[52]

The trocars used with the Prolift device made it easier to affix the vagina to deep structures that can be difficult to access without such tools. The fact that the mesh was pre-cut for an anterior, posterior, or total repair was also helpful and useful. The device allowed the surgeon to reinforce a prolapse repair with a durable mesh graft in a minimally invasive surgery .

All surgical procedures have inherent risks. All pelvic surgeries have similar risks, and the introduction of the Gynemesh PS mesh and the Prolift device has served to decrease complications when compared to previous techniques. Because native repairs do not involve a kit product, complications are not reportable to the MAUDE database. Scientific research has provided improved materials and applications to both improve efficacy and decrease complications. Synthetic mesh that is microporous or too macroporous has proven to be either less safe or less efficacious. If the mesh is too lightweight or too large pore, there is inadequate support.

All pelvic surgery has similar and inherent risks. Pelvic floor surgeons should be and are aware of the potential complications involved with any surgical treatment of pelvic organ prolapse based on a combination of their medical school education, their residencies, fellowships, their experience, their continuing education, and their review of the device's IFU if a surgical mesh device is used. Risks such as infection, scarring, inflammation, bladder damage, bowel damage, ureter damage, nerve damage, injury to vessels, wound complications (such as wound dehiscence, herniation, hematoma, seroma, pelvic abscess, exposure, and erosion), pain, pelvic pain, groin pain, dyspareunia, fistula, anesthetic risks, bowel or bladder dysfunction, failure of the operation, bleeding, death, pulmonary embolism, myocardial infarction, pneumonia, deep vein thrombosis, and need for reoperation are basic elemental surgical risks of any pelvic floor surgery involving mesh. Surgeons understand that these complications can happen, and they also understand that the symptoms can range in terms of severity and duration.

Surgeons are expected to understand the anatomy in which they are operating, and should identify and dissect in safe planes, avoiding inadvertent damage to the organs and vessels contained within the pelvis. The education and training of the pelvic surgeon should be adequate to know the possibility of complications and their avoidance, risks of recurrence and reoperation. Indeed, the development of biologic and synthetic materials was motivated by the high failure rate of pelvic reconstruction due to the weakness of the patients' connective tissue leading to the condition requiring repair. There is an extensive body of medical knowledge in the medical literature discussing the possibility of complications with the use of meshes. Surgeons' prior experience with mesh informs their understanding of potential complications with pelvic floor surgeries, including those involved with mesh devices. While mesh exposure is unique to mesh devices, it is obvious, and it is general knowledge within female urology and urogynecology. The potential injury to vessels and organs caused by trocars is well-known to surgeons, and potential mesh exposure and foreign body reactions are common knowledge.

[52] Abed H, et al., Incidence and management of graft erosion, wound granulation, and dyspareunia following vaginal prolapse repair with graft materials: a systematic review. Int Urogynecol J 2011 Jul;22(7):789–798.

Furthermore, the FDA issued a Public Health Notification in 2008 regarding the use of synthetic mesh for treatment of prolapse and incontinence. It alerted healthcare practitioners to "complications associated with transvaginal placement of surgical mesh to treat Pelvic Organ Prolapse (POP) and Stress Urinary Incontinence (SUI)." It noted that the major complications were rare, but could have serious consequences, and that the "most frequent complications included erosion through the vaginal epithelium, infection, pain, urinary problems, and recurrence of prolapse and/or incontinence." It also noted that there were "reports of bowel, bladder, and blood vessel perforation during insertion," and that "[i]n some cases, vaginal scarring and mesh erosion led to a significant decrease in patient quality of life due to discomfort and pain, including dyspareunia." This Public Health Notification was yet another source of knowledge for surgeons regarding potential complications associated with synthetic mesh midurethral slings, complementing the Prolift's IFU, Ethicon's professional education seminars, and the surgeons' training, education, and experience.

Based upon the analysis above, and on my education, my training, my experience using these products and alternative incontinence treatments, and my reading of the literature referenced above, I believe that Ethicon's Prolift device is not defective, but was reasonably safe for its intended use and had a positive benefit-to-risk profile. It provided better anatomic support than native tissue repairs, and most patients were very satisfied with the Prolift procedure. Recovery times and operative times were minimal, success rates were high, and complication rates were low with the Prolift device. In my opinion, the benefits of the Prolift device outweighed the risks of using the product. At the time the product was launched, I do not believe it could have been made safer for its intended use. The product was state of the art at the time it was launched.

Date: 2/29/16

Douglas H. Grier, M.D.

Exhibit C

Report re TVT and TVT-O Mid-urethral Slings

Douglas H. Grier, M.D.
Sound Urological Associates, P.S.
21822 76th Ave., W
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This report contains a summary of my qualifications, education, training, and experience, a statement of my opinions that I have formed to date, the bases for those opinions, and the information I considered in forming my opinions. All of my opinions are based on my education, training, clinical experience, the pertinent medical literature, discussions with colleagues, and other materials I have reviewed. Materials that support my findings and opinions, including documents that I have reviewed, are identified either in this report or are listed in the attached reliance materials list.

All of the opinions I express in this report are held to a reasonable degree of medical and scientific certainty. If I receive additional information after signing this report but before trial, I may form additional or different opinions.

I. Background

a. Education, Training, and Experience

I attended the University of Florida in Gainesville, Florida, graduating with a Bachelor of Science degree in Chemistry with High Honors in 1976. I attended medical school at George Washington University, graduating in 1982. I then did a surgical internship in 1982–1983 at the Portsmouth Naval Hospital in Portsmouth, Virginia. Following my internship, I did a urological residency at the Portsmouth Naval Hospital from 1984–1988. I served as Chief of Urology at Jacksonville Naval Hospital in 1990-91.

Prior to my residency, I served in Operation Urgent Fury in Grenada in October 1983 and as part of the Multinational Peacekeeping Force in Beirut, Lebanon in 1983–1984. After my residency, I served in Operation Desert Shield and Operation Desert Storm with the 1st Marine Division, stationed in Saudi Arabia and Kuwait in 1990–1991.

I am the President-Elect of the Medical Staff at Swedish/Edmonds Hospital in Edmonds, Washington. I also serve as the Chair of Swedish Hospital's Medical Quality Oversight Committee, Chair of the Credentials Committee, Treasurer of the Medical Staff for the Swedish Hospital System, and as a member of the Executive Committee at Swedish Hospital.

I became a Diplomate of the American Board of Urology in 1990 and was recertified in 2010. I am an active member of the American Urological Association, the Washington State Medical Association, the Northwest Urological Society, the Washington State Urology Society, the King County Medical Society, the American Association of Clinical Urologists, the Society of Urodynamics Female Pelvic Medicine & Urogenital Reconstruction, and the International Continence Society.

My curriculum vitae is attached to this report.

b. Clinical Experience & Personal Experience with Stress Urinary Incontinence Treatments

I have a special focus in female pelvic medicine and surgery. Over the course of my career, I have performed various types of native tissue surgery and surgery utilizing mesh, including Ethicon's TVT and TVT-O, TVT-Abbrevo, and TVT-Secur mid-urethral slings, AMS Monarch, Uretex by Bard, Vesica In situ sling, Stamey cystourethropexy, MMK, and Burch procedures. I have also performed robotic sacrocolpopexies, as well as open abdominal sacrocolpopexies. I have also performed various types of native tissue surgeries and surgeries utilizing mesh to treat pelvic organ prolapse and hernias.

c. Teaching & Training Experience Related to Stress Urinary Incontinence

I served as a faculty member at the Ethicon Endosurgical Institute, and as a National Preceptor for Gynecare products, conducting over 300 courses for advanced surgical training of physicians for conditions such as stress urinary incontinence and pelvic organ prolapse. I have lectured to pelvic floor surgeons throughout the United States, Canada, Europe, and China. I have performed research in the field of incontinence and bladder disorders, contributing to studies on the use of TVT abdominal guides, and the TVT world registry published in the Journal of Urology in 2011. I was also an investigator in an FDA trial of a pelvic nerve stimulator for the treatment of urge incontinence.

d. Litigation Consulting Work

During the previous four years, I have testified as an expert witness at trial or by deposition in the following case:

- Perry v. Ethicon, Inc., et al.—Bakersfield, CA
  - Deposition Testimony on 12/30/14
  - Trial Testimony on 02/17/15, 02/18/15, and 02/19/15

I am being compensated $500 per hour for my study and testimony in this case.

II. Stress Urinary Incontinence

a. Definition, Mechanism of Action, and Prevalence

Urinary incontinence is the involuntary leakage of urine, and can take different forms such as urge incontinence, stress incontinence, or mixed incontinence. Urinary incontinence affects up to 50% of women at some point in their lives. (Ford AA, Rogerson L, Cody JD, Ogah J. Mid-urethral sling operations for stress urinary incontinence in women. Cochrane Database of Systematic Reviews 2015, Issue 7. Art. No.: CD006375. DOI: 10.1002/14651858.CD006375.pub3.) Stress Urinary Incontinence ("SUI") is the involuntary leakage of urine during activities such as coughing, sneezing, lifting, laughing, or exercising.

(IUGA Stress Urinary Incontinence – A Guide for Women.) The proposed mechanism of action for the development of stress urinary incontinence is weakening of the pubourethral ligaments and loss of intrinsic sphincter tone.

SUI is diagnosed by bladder questionnaire, examination, cough test, bladder diary, urodynamic studies, and cystoscopy. Pelvic organ prolapse, overactive bladder, and urinary incontinence affect more women than diabetes, heart disease, or arthritis. SUI is a very common condition, and affects at least 10–35% of women. (IUGA Stress Urinary Incontinence – A Guide for Women; Dooley Y, et al., Urinary incontinence prevalence: results from the National Health and Nutrition Examination Survey. J Urol 2008 Feb;179(2):665–661.) A recent Cochrane review notes that, of the 50% of women who will experience urinary incontinence at some point in their lives, 30–80% experience SUI. (Ford AA, Rogerson L, Cody JD, Ogah J. Mid-urethral sling operations for stress urinary incontinence in women. Cochrane Database of Systematic Reviews 2015, Issue 7. Art. No.: CD006375. DOI: 10.1002/14651858.CD006375.pub3.) Moderate-to-severe SUI affects women at an increasing rate as they age, and has been reported to affect 6.9% of women 20–39 years old, 17.2% of women 40–59 years old, 23.3% of women aged 60–79 years, and 31.7% of women 80 years or older. (Nygaard I, et al., Prevalence of symptomatic pelvic floor disorders in US women. JAMA 2008 Sep 17;300(11):1311–1316.) One study estimated that approximately 11% of women will have surgery to treat either SUI or pelvic organ prolapse in their lifetime. (Olsen AL, et al., Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. Obstet Gynecol 1997;89:501-506.) Over 200,000 surgeries are performed in the U.S. for the treatment of SUI and pelvic organ prolapse each year. (Gerten KA, et al., Prolapse and incontinence surgery in older women. J Urol 2008 Jun;179(6):2111–21118.)

b. Risk Factors for Stress Urinary Incontinence

Smoking: Women who smoke are 1.8–2.9 times more likely to develop SUI. (Bump RC, Am. J. Obstet. & Gynecol 1992;167:1213–1218.) Smoking can lead to COPD, which increases abdominal pressures through chronic coughing.

Obesity: Increasing body mass index correlates to an increase in the symptoms of urinary incontinence and pelvic organ prolapse through the mechanism of increased intravesical pressure and bladder receptor changes. (Hannestad YS, et al., Are smoking and other lifestyle factors associated with female urinary incontinence? The Norwegian EPINCONT Study. Br J Obstet Gynaecol 2003 Mar;110(3):247–254.) Obese women have a 4.2-fold greater risk of developing SUI compared to women with an average BMI. (ACOG / AUGS Practice Bulletin No. 155; Nov. 2015.)

Menopause: Decreasing serum levels of estrogen are known to increase the incidence of both stress incontinence and integrity of the pubocervical fascia of the vagina by decreasing vascularity and thickness of the tissues. Postmenopausal decreased estrogen levels lead to urogenital atrophy with the increased risk of infections of the urinary tract and changing of the vaginal pH. (Siddighi S & Hardesty JS, Urogynecology & Female Pelvic Reconstructive Surgery. ISBN 0-07-144799-7.)

Pregnancy and Childbirth: Damage sustained to the muscles and nerves of the pelvic floor significantly increases the risk of both stress and urge incontinence and pelvic organ prolapse. A woman with three or more vaginal deliveries has an eleven-fold increased risk of pelvic organ prolapse compared to a nulliparous woman. The weight of the infant contributes to prolapse with an increase of 10% per pound weight of the infant. (Siddighi S & Hardesty JS, Urogynecology & Female Pelvic Reconstructive Surgery. ISBN 0-07-144799-7.)

Chronic Constipation and Heavy Lifting: Chronic constipation and heavy lifting cause increased pelvic pressures which leads to increased fascial stress over time.

Race: Increasing incidence of SUI occurs from Asian women < African-American women < Caucasian Women. Caucasian women have the highest risk of pelvic organ prolapse. (Siddighi S & Hardesty JS, Urogynecology & Female Pelvic Reconstructive Surgery. ISBN 0-07-144799-7.)

Age: The mean age for SUI in women is 48 years, for mixed incontinence in women 55 years, and urge incontinence in women is 61 years. The prevalence of incontinence is 39.6 million women as of 2001. (Siddighi S & Hardesty JS, Urogynecology & Female Pelvic Reconstructive Surgery. ISBN 0-07-144799-7.)

Congenital Factors: Women with prolapse tend to have an abundance of the weaker type III collagen in the pubocervical fascia with a higher degree of joint hypermobility with associated collagen vascular disorders. These factors also increase the incidence and severity of prolapse. Collagen vascular diseases have been implicated in the development of SUI and pelvic organ prolapse. (Siddighi S & Hardesty JS, Urogynecology & Female Pelvic Reconstructive Surgery. ISBN 0-07-144799-7.)

Pelvic Organ Prolapse: 62% of women with prolapse also report SUI and 63% of women with stress incontinence have associated prolapse. (Siddighi S & Hardesty JS, Urogynecology & Female Pelvic Reconstructive Surgery. ISBN 0-07-144799-7.)

c. Economic Impact and Impact on Quality of Life

Women who develop urinary incontinence adapt by minimizing activities, wearing incontinence diapers, and by avoiding social interactions and sexual relationships due to fear of embarrassment. (Fultz NH, et al., Burden of stress urinary incontinence for community-dwelling women. Am J Obstet Gynecol 2003 Nov;189(5):1275–1282.) It has been reported that less than half of women who experience incontinence tell their healthcare providers about their symptoms. (Wu JM, et al., Prevalence and incidence of urinary incontinence in a diverse population of women with noncancerous gynecologic conditions. Female Pelvic Med Reconstr Surg 2010;16(5):284–289; ACOG / AUGS Practice Bulletin No. 155; Nov. 2015.) The impact of decreased physical activities for fear of incontinence leads to cardiovascular deconditioning, further obesity, and social isolation. The incontinence also increases the incidence of urinary tract infections, which can lead to kidney infections and hospitalizations. The symptoms of SUI can also increase the incidence and severity of depression.

62% of women with prolapse also report SUI and 63% of women with stress incontinence have associated prolapse. (Gallentine ML and Cespedes RD, Occult stress urinary incontinence and the effect of vaginal vault prolapse on abdominal leak point pressures. Urology 2001 Jan;57(1):40-44.) 30% of women will undergo repeat surgery for recurrent prolapse over their lifetime.

Economic costs of urinary incontinence were estimated to be $32 billion as of 2000, with the cost derived from providing laundry, pads, and absorbent products. The majority of those costs do not come from providing treatment. The November 2015 ACOG/AUGS Practice Bulletin on Urinary Incontinence in Women notes that the "estimated direct cost of urinary incontinence care in the United States is $19.5 billion." (ACOG / AUGS Practice Bulletin No. 155; Nov. 2015.) 62% of women with prolapse also report SUI and 63% of women with stress incontinence have associated prolapse. (Siddighi S & Hardesty JS, Urogynecology & Female Pelvic Reconstructive Surgery. ISBN 0-07-144799-7; Wagner, Economic Costs of Urinary Incontinence, Urology 1998;51:355–361.)

III. Treatment Options for SUI

a. Nonsurgical Options for Treatment of Stress Urinary Incontinence

Nonsurgical treatment options for SUI are behavior modifications, including more frequent voiding, incontinence pads or briefs, biofeedback, pelvic floor muscle exercises, weight reduction, management of fluid intake, smoking cessation, reduced intake of coffee, tea, and carbonated beverages, reduced occupational or recreational activities that require repetitive or chronic straining, and constipation management. Other nonsurgical treatment options include functional electrical stimulation (PTNS) and mechanical devices. (Siddighi S & Hardesty JS, Urogynecology & Female Pelvic Reconstructive Surgery. ISBN 0-07-144799-7; ACOG / AUGS Practice Bulletin No. 155; Nov. 2015.) Only 15–28% of women have their incontinence 100% cured by pelvic floor muscle training (PFMT), and after a 3–15-year follow-up, 25–50% of women primarily treated with PFMT to try to improve or cure their incontinence will undergo surgery. (Labrie J, et al., Protocol for Physiotherapy OR Tvt Randomised Efficacy Trial (PORTRET): a multicenter randomised controlled trial to assess the cost-effectiveness of the tension free vaginal tape versus pelvic floor muscle training in women with symptomatic moderate to severe stress urinary incontinence. BMC Women's Health 2009;9:24.)

Pessaries are believed to control SUI symptoms by increasing urethral resistance and supporting the urethra. They "may improve the symptoms of stress and mixed urinary incontinence, but objective evidence regarding their effectiveness has not been reported." (ACOG / AUGS Practice Bulletin No. 155; Nov. 2015.)

The limitations of nonsurgical management options are that they rarely fully restore continence, but rather help cope with the condition. There is no FDA-approved medication for the treatment of SUI. (ICS Fact Sheets: A Background to Urinary and Faecal Incontinence (July 2013); 2013 AUA SUI Patient Guide.)

b. Surgical Options for Treatment of Stress Urinary Incontinence

Because of the limitations of nonsurgical treatment options, surgery is the definitive and long-term treatment for symptomatic SUI. There are over 150 described surgical treatments for SUI. All of these surgeries have shared risks such as hematoma, bladder or bowel injury, lower urinary tract injury, vascular injury, infection, urinary retention, persistent SUI, bleeding, pain, dyspareunia, fistula, and de novo or worsening urge incontinence. (ACOG / AUGS Practice Bulletin No. 155; Nov. 2015.)

i. Native Tissue and Tension Repairs

The primary surgical native tissue and tension repairs include the Kelly plication (introduced in 1912), Pereyra needle urethropexy (introduced in 1959), and abdominal operations for SUI such as the Burch colposuspension (introduced in 1961) and Marshall Marchetti Krantz (MMK) cystourethropexy (introduced in 1949). (Siddighi S & Hardesty JS, Urogynecology & Female Pelvic Reconstructive Surgery. ISBN 0-07-144799-7.)

Retropubic trans-abdominal surgeries (Burch and MMK) when compared to TVT, are less cost-effective, more morbid, have greater operative time, and longer recovery with equal efficacy. (Ward K, et al., Prospective multi-center randomized trial of tension-free vaginal tape and colposuspension as primary treatment for stress incontinence. BMJ 2002 Jul;325:1–7.) In a randomized controlled trial of TVT versus Burch with five-year follow-up, the procedures had similar patient satisfaction and efficacy, but the TVT group had less voiding dysfunction. (Ward K and Hilton P on behalf of the UK and Ireland TVT Trial Group, Tension-free vaginal tape versus colposuspension for primary urodynamic stress incontinence: 5-year follow up. BJOG 2008;115:226–233.) A 2009 Cochrane review of TVT versus Burch reported that TVT appeared to be as effective as the open Burch procedure, but associated with fewer complications, less voiding dysfunction, shorter operative times, and increased safety. (Ogah, J., Cody, JD, Rogerson, L., Minimally invasive synthetic suburethral sling operations for stress urinary incontinence in women. Cochrane Database of Systematic Reviews 2009, Issue 4. Art. No.: CD006375. DOI:10.1002/14651858.CD006375.pub2.) A meta-analysis of 39 RCTs published in 2010 by Novara, et al. indicated that patients receiving midurethral slings, especially TVT, while having an increased risk of bladder perforation, had significantly higher overall and objective cure rates than did the patients who had a Burch procedure. (Novara G, et al. Updated systematic review and meta-analysis of the comparative data on colposuspensions, pubovaginal slings, and midurethral tapes in the surgical treatment of female stress urinary incontinence. Eur Urol 2010 Aug;58(2):218-38.)

Retropubic trans-abdominal surgeries such as the Burch and MMK involve larger incisions, more dissection, are performed as inpatient rather than ambulatory procedures, and have a greater average blood loss than the mid-urethral sling procedures discussed below. (Chaliha C, Stanton SL. Complications of surgery for genuine stress incontinence. Br J Obstet Gyaecol. 1999 Dec;106(12):1238–45.) Data shows that long-term efficacy following Burch declines with time and plateaus at ten years with 70% cure. One in ten patients needs at least one additional surgery for correction of SUI ten years after undergoing a Burch procedure. (Alcalay, Burch colposuspension: a 10-20 year follow up. Br J Obstet Gynaecol 1995;102:740-745.) In

another long-term study of the Burch procedure, 56% of the patients studied experienced subjectively significant urinary incontinence. (Kjolhede P, Long-term efficacy of Burch colposuspension: a 14-year follow-up study, Acta Obstet Gynecol Scand 2005, 84:767-772.) In the SISTEr study, 70% of patients undergoing the Burch procedure had treatment failure at two years' follow-up when all criteria were considered. (Albo, ME, et al., Burch Colposuspension versus Fascial Sling to Reduce Urinary Stress Incontinence, N Engl J Med 2007;356:2143-2155.) In the extended SISTEr trial, between 2–7 years post-op continence rates dropped from 42% to 13% in patients who had the Burch procedure. (Richter HE, et al., Patient Related Factors Associated with Long-Term Urinary Continence After Burch Colposuspension and Pubovaginal Fascial Sling Surgeries. J Urol 2012 Aug;188(2):485–489.) A study by Demirci showed comparable trends in decreasing efficacy and late complications. Demirci reported late complications in 220 women, including enterocele (35), rectocele (32), cystocele (18), suprapubic or groin pain (15), and dyspareunia (6). (Demirci F, et al. Long-term results of Burch colposuspension. Gynecol Obstet Invest. 2001;51(4):243-7.)

Laparoscopic Burch procedures have a lower cure rate, higher complication rate, and higher operative cost than open Burch procedures. (Siddighi S & Hardesty JS, Urogynecology & Female Pelvic Reconstructive Surgery. ISBN 0-07-144799-7; Walters, Surgical management of stress incontinence, Clinical Obstetrics & Gynecology-Incontinence. Lipincott William & Wilkins 2004:93–103.) A 2012 Cochrane Review reported that there was insufficient evidence to determine whether the laparoscopic Burch procedure has an advantage over the open Burch procedure in terms of cost-effectiveness, longer-term complications, safety, quality of life, and subjective and objective cure rates. (Lapitan MC, Cody JD. Open retropubic colposuspension for urinary incontinence in women. Cochrane Database Syst Rev 2012 Jun 13.)

In the SISTEr trial, 47% of the patients undergoing the Burch procedure experienced adverse events. (Albo, ME, et al., Burch Colposuspension versus Fascial Sling to Reduce Urinary Stress Incontinence, N Engl J Med 2007;356:2143-2155.) Urinary retention rate after Burch is 12%. De novo detrusor overactivity is 16% post-operatively. 25-45% patients with mixed incontinence pre-op will have worse detrusor overactivity post-op. There is a 7–14% risk of enterocele (prolapsed small intestine) formation. 12% have post-colposuspension syndrome, which is chronic pain in the low-to-mid pelvis due to the Burch suture tension. (Siddighi S & Hardesty JS, Urogynecology & Female Pelvic Reconstructive Surgery. ISBN 0-07-144799-7.) Osteitis pubis—which is inflammation of the periosteum from the sutures—occurs at a rate of 2-3%. Dyspareunia increases when combined with vaginal prolapse surgery. Urinary tract infections and wound complications also occur. (Siddighi S & Hardesty JS, Urogynecology & Female Pelvic Reconstructive Surgery. ISBN 0-07-144799-7.) The Alcalay study reported that 14.7% of the patients had detrusor instability, 22% had long-term voiding difficulty, and 4.6% had recurrent urinary tract infections. The AUA 2012 Update to the SUI Guidelines reported higher rates of pain and sexual dysfunction with the Burch procedure than with midurethral slings. (Guideline for the Surgical Management of Female Stress Urinary Incontinence: 2009 Update Appendices A11 and A16.) The significant post-operative morbidity and complications associated with the Burch procedure has caused surgeons to turn to other procedures to treat SUI. (Wu CJ, et al., The surgical trends and time-frame comparison of primary surgery for stress urinary incontinence, 2006-2010 vs 1997-2005: a population-based nation-wide follow-up descriptive study. Int Urogynecol J 2014 Dec;25(12):1683–91; Chughtai BI, et al., Midurethral

Sling Is the Dominant Procedure For Female Stress Urinary Incontinence: Analysis of Case Logs From Certifying American Urologists. Urology 2013 Dec;82(6):1267–71; Suskind AM, et al., Effectiveness of Mesh Compared with Nonmesh Sling Surgery in Medicare Beneficiaries. Obstet Gynecol 2013 Sep;122(3):546–52; Rogo-Gupta L, et al., Trends in the Surgical Management of Stress Urinary Incontinence Among Female Medicare Beneficiaries, 2002-2007. Urology 2013 Jul;82(1):38–41; Nager CW, et al., A Randomized Trial of Urodynamic Testing before Stress-Incontinence Surgery. N Engl J Med 2012 May;24;366(21):1987–97; Wu JM, et al., Trends in inpatient urinary incontinence surgery in the USA, 1998-2007. Int Urogynecol J 2011 Nov;22(11):1437–43.)

Retropubic needle suspensions have been essentially abandoned due to high failure rates, and share all of the risks discussed above with respect to retropubic trans-abdominal surgeries.

ii. Bulking Agents

Bulking agents are another option for treatment of SUI. They can be made of bovine collagen or polytetrafluoroethylene (PTFE), and are needle-injected into the urethral submucosa to coapt the urethra. Advantages of these procedures include the fact that they can be office-based, they do not require general anesthesia, they can be performed in patients who are not surgical candidates, and they can be used after failed previous surgeries. While bulking agents are invasive, they are less invasive than other surgical options. Drawbacks of bulking agents include high cost, lower cure rates—25% dry, 50% improved, and 25% requiring repeat injections. Complications include urinary retention (15-25%), urinary tract infection (5-30%), irritative voiding symptoms (less than 20%), allergic reactions (4%), and product migration. (Gross M, et al., Periurethral injections. In: Bent AE, et al., eds. Ostergard's Urogynecology and Pelvic Floor Dysfunction 5th ed. William & Wilkins; 2003:495–502.) "[U]rethral bulking agents are less effective than surgical procedures such as sling placement and are rarely used as primary treatment for stress urinary incontinence." (ACOG / AUGS Practice Bulletin No. 155; Nov. 2015.)

iii. Artificial Urinary Sphincters

Artificial urinary sphincters are inflatable cuffs that surround the proximal urethra and bladder neck. They provide mechanical obstruction of the urethra when inflated and allow opening with activation of a control pump. Due to the extensive surgery required and long-term complications of device failure (e.g., pump failure, urethral erosion, infection), artificial sphincters are used for severe incontinence when other procedures have failed. (Appell, Techniques and results in the implantation of the artificial urinary sphincter in women with type 3 SUI with vaginal approach. Neurourol Urodyn 1988;7:613–619.)

iv. Proximal Suburethral Slings

Another surgical treatment option for SUI is the proximal suburethral sling. Originally used only for intrinsic sphincter deficiency ("ISD") and recurrent stress incontinence because of the higher post-operative complications, proximal suburethral slings create a hammock underneath the urethra and bladder neck to prevent descent and provide a backboard for

compression of the urethra during increased intra-abdominal pressure. First described in 1907, several biologic and synthetic materials have been used, and bone-anchored slings have also been developed. The biologic materials used include autografts (fascial tissue removed from the patient's abdomen (rectus fascia) or outer thigh (fascia lata)), allografts (sterilized fascia from a cadaver), or xenografts (sterilized fascia from an animal). Modification of the suburethral slings by anchoring to the pubic bone does not increase effectiveness, and carries an increased risk of osteomyelitis. Overall success is between 82–90% at 5 years. Cure rates for SUI with ISD at 5 years is 80–90%, which is higher than Burch. However, In the SISTEr study, 57% of patients receiving a fascial sling had treatment failure at two years' follow-up when all criteria were considered. (Albo, ME, et al., Burch Colposuspension versus Fascial Sling to Reduce Urinary Stress Incontinence, N Engl J Med 2007;356:2143-2155.) In the extended SISTEr trial, between 2–7 years post-op continence rates dropped from 52 to 27% in patients who had pubovaginal slings. (Richter HE, et al., Patient Related Factors Associated with Long-Term Urinary Continence After Burch Colposuspension and Pubovaginal Fascial Sling Surgeries. J Urol 2012 Aug;188(2):485–489.) The 2014 SGS systematic review and meta-analysis by Shimpf et al. observed that, when comparing pubovaginal slings versus midurethral slings, subjective cure was higher with midurethral slings. Therefore, the authors recommended midurethral slings over pubovaginal slings. (Schimpf MO, et al., Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. Am J Obstet Gynecol 2014;210:1.e1-1.e27.)

Cure rates may be high, but complication rates are also higher with these procedures. These procedures are highly morbid, involve abdominal and transvaginal incisions, greater operative time, more blood loss, more transfusions, autologous fascia has to be harvested from the patient using a separate incision, recovery time is much longer than other surgical treatment methods, and the complication rate is higher in terms of urinary retention, possible bone anchoring complications, hematoma, chronic pain, infection, exposure, and de novo urinary detrusor overactivity. (Chaikin DC, et al., Pubovaginal fascial sling for all types of stress urinary incontinence: long-term analysis. J Urol 1998 Oct;160(4):1312–1316; Schimpf MO, et al., Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. Am J Obstet Gynecol 2014;210:1.e1-1.e27; Brubaker L, 5-Year Continence Rates, Satisfaction and Adverse Events of Burch Urethropexy and Fascial Sling Surgery for Urinary Incontinence, Urology 2012;187:1324-1330; Richter HE, et al., Patient Related Factors Associated with Long-Term Urinary Continence After Burch Colposuspension and Pubovaginal Fascial Sling Surgeries, Urology 2012;188:485-489; Albo, ME, et al., Burch Colposuspension versus Fascial Sling to Reduce Urinary Stress Incontinence, N Engl J Med 2007;356:2143-2155; Rehman H, et al., Traditional suburethral sling operations for urinary incontinence in women. Cochrane Database Syst Rev. 2011 Jan 19;(1):CD001754. Doi: 10.1002/14651858.) In the SISTEr trial, 63% of the patients receiving fascial slings experienced adverse events. (Albo, ME, et al., Burch Colposuspension versus Fascial Sling to Reduce Urinary Stress Incontinence, N Engl J Med 2007;356:2143-2155.) The AUA 2012 Update to the SUI Guidelines reported higher rates of pain and sexual dysfunction with pubovaginal slings than with midurethral slings. (Guideline for the Surgical Management of Female Stress Urinary Incontinence: 2009 Update Appendices A11 and A16.) Harvesting autologous fascia from the abdomen or outer thigh carries a risk of pain, nerve entrapment, and infection, which is a significant drawback to the procedure. The American College of Obstetricians and Gynecologists and the American Urogynecologic Society recommend that autologous fascial bladder neck slings be considered for women who decline or

are not candidates for synthetic mesh slings. (ACOG / AUGS Practice Bulletin No. 155; Nov. 2015.) Using allografts and xenografts can be met with cultural or religious objections from patients, and carries a risk of disease transmission and rejection. Allografts and xenografts are also more costly than other materials, and lack the long-term durability of synthetic materials.

v. Midurethral Tension-Free Slings

Midurethral tension-free slings were developed by Ulmsten in Sweden in the 1980s to mid-'90s due to the high morbidity and unpredictable success of retropubic or proximal urethral suspension procedures. These procedures involve the placement of a tension-free synthetic midurethral sling that can be placed either retropubic or transobturator. They act as a hammock or backstop for the midurethra during the moments of increased bladder pressure caused by physical activity. Indications for midurethral slings are SUI with hypermobility of the urethra, SUI with ISD, mixed incontinence with stress predominance, and recurrent SUI following failed previous procedures. They have been used extensively in Europe for the treatment of SUI, became popular in the U.S. in the late 1990s, and have revolutionized the treatment of SUI. (Siddighi S & Hardesty JS, Urogynecology & Female Pelvic Reconstructive Surgery. ISBN 0-07-144799-7.) The majority are performed in ambulatory centers with minimal incision and without the requirement for post-operative catheterization. Other advantages are that it is a shorter learning curve for the surgeon (which means more women have access to the treatment), and involve less post-operative pain for the patient. Most pelvic floor surgeons prefer synthetic mid-urethral slings to traditional procedures in most circumstances. (Clemons JL, et al., Impact of the 2011 FDA Transvaginal Mesh Safety Update on AUGS Members' Use of Synthetic Mesh and Biologic Grafts in Pelvic Reconstructive Surgery. Female Pelvic Med Reconstr Surg 2013;19:191-198; Chughtai BI, et al., Midurethral Sling Is the Dominant Procedure for Female Stress Urinary Incontinence: Analysis of Case Logs From Certifying American Urologists. Urology 2013 Dec;82(6):1267–71; Nager CW, et al., A Randomized Trial of Urodynamic Testing before Stress-Incontinence Surgery. N Engl J Med 2012 May 24;366(21):1987–1997.)

IV. Ethicon TVT Products

a. Historical Background of Surgical Use of Mesh

Polypropylene sutures have been used for over 45 years and are biologically compatible with human tissue. Polypropylene hernia mesh has been and continues to be the standard of care for the last thirty years for abdominal wall hernia repair. Polypropylene mesh has been used in open abdominal sacrocolpopexies since the 1960s. The advantage of mesh is augmentation and strength during the healing process with the incorporation of collagen fibers into the material to provide lasting support. I have been performing polypropylene mesh hernia repairs since the 1980s and have never had a patient develop an infection or rejection of the material.

b. The Development of Tension-Free Vaginal Tape Using Prolene Mesh

As mentioned above, midurethral tension-free slings were developed by Ulmsten in Upsala, Sweden in the 1980s to mid-1990s, at which time he and Dr. Petros experimented with multiple different available materials for the slings, including Mersilene, Marlex, Prolene, Gore-

Tex, and others. (Petros PE, Creating a gold standard surgical device: scientific discoveries leading to TVT and beyond: Ulf Ulmsten Memorial Lecture 2014. Int Urogynecol J 2015 Apr;26(4):471-6; Ulmsten U, et al. A multicenter study of tension-free vaginal tape (TVT) for surgical treatment of stress urinary incontinence. Int Urogynecol J Pelvic Floor Dysfunct 1998;9(4):210-213; Petros PE, Ulmsten UI, An integral theory and its method for the diagnosis and management of female urinary incontinence. Scand J Urol Nephrol Suppl 1993;153:1-93.) Dr. Ulmsten and Dr. Petros selected the monofilament, large-pore, knitted, lightweight Prolene mesh due to Prolene's long-term use in surgery as a suture material, its ease of use, and its biocompatibility in the vagina. Dr. Ulmsten also determined that a Prolene sling that was 1 centimeter in width and 40 centimeters in length was optimal. The width of the sling was eventually changed to 1.1 cm, and the length was subsequently increased to 45 cm to facilitate treatment of more women. Dr. Axel Arnaud of Ethicon went to Sweden in 1995 and observed four of Ulmsten's tension-free procedures and negotiated with Ulmsten to purchase the rights to the product he had developed. The TVT has been used extensively in Europe for the treatment of SUI and was introduced to the U.S. in 1998, becoming the gold standard for SUI surgery over the next several years.

c. The TVT and TVT-O Devices

The TVT is a monofilament, knitted, macroporous, lightweight, synthetic mesh sling that is swedged onto trocars that are passed at the midurethra via a 1.5 cm vaginal incision under the pubic symphysis and emanating approximately 2 cm lateral from the midline of the abdomen, just above the pubic symphysis. The mesh is encased in a plastic sheath that is removed after deployment of the mesh. The sling is not anchored; it is placed without tension under the mid-urethra, and a cough test is then performed to assess the degree of continence provided by the sling. The ends of the sling are cut beneath the surface of the skin on the abdominal wall after tensioning, and the vaginal incision is closed with an absorbable suture. Cystoscopy is performed to insure the bladder is not perforated by the sling during its deployment. The device comes in a box with the above-mentioned components, along with instructions for use for the device. Internationally, the TVT is the most common midurethral synthetic sling that is utilized. The TVT has the longest studies available that have demonstrated both low complication rates and high efficacy, with studies carried out as long as seventeen years. (Nilsson CG, et al., Seventeen years' follow-up of the tension-free vaginal tape procedure for female stress urinary incontinence. Int Urogynecol J 2013 Aug;24(8):1265–1269. doi 10.1007/s00192-013-2090-2.) The TVT is more cost effective, uses less operative time, and has a higher objective cure rate (at less than two years) than the laparoscopic Burch colposuspension. Compared to open Burch procedure, the TVT has a similar cure rate for up to two years of treatment, but is less costly and involves less recovery time. (Siddighi S & Hardesty JS, Urogynecology & Female Pelvic Reconstructive Surgery. ISBN 0-07-144799-7.)

The TVT-O, like the TVT, is a monofilament, knitted, macroporous, synthetic mesh sling that is swedged onto trocars that are passed at the midurethra via a 1.5 cm vaginal incision and through the obturator foramen and out the medial thigh. The same Prolene mesh is used in both the TVT and TVT-O slings. The mesh is a Type I mesh, per the biomaterial classification published by PK Amid in 1997, as it contains pores larger than 75 microns, "which is the required pore size for admission of macrophages, fibroblasts (fibroplasia), blood vessels

(angiogenesis) and collagen fibers into the pores." (Amid PK, Classification of biomaterials and their related complications in abdominal wall hernia surgery. Hernia 1997;1:15–21.) Like the TVT, the mesh of the TVT-O is encased in a plastic sheath that is removed after deployment of the mesh. The sling is not anchored; it is placed without tension, and a cough test is performed to assess the degree of continence provided by the sling. The ends of the sling are cut beneath the surface of the skin on the medial thigh after tensioning, and the vaginal incision is closed with an absorbable suture. It is recommended that cystoscopy be performed following the procedure, but I have found it to be optional due to the decreased likelihood of perforation of the bladder. The device comes in a box with the above-mentioned components along with instructions for use for the device. Hundreds of thousands of TVT-O procedures have been performed internationally since its introduction. It was first introduced in North America in 2004, and I performed the first case in North America in January 2004. The advantage of the transobturator approach is less risk of bladder perforation, retropubic hematoma, and possible bowel injury by avoiding the space of Retzius. The TVT-O procedure has a short learning curve, low morbidity, and a short operating time, and is technically simple to perform, which makes the procedure available to more women. (Groutz A, et al., Long-Term Outcome of Transobturator Tension-Free Vaginal Tape: Efficacy and Risk Factors for Surgical Failure. J Women's Health 2010;20(10):1525–1528.) There are several long- or intermediate-term studies of the TVT-O supporting its safety and efficacy. (Groutz A, et al., Long-Term Outcome of Transobturator Tension-Free Vaginal Tape: Efficacy and Risk Factors for Surgical Failure. J of Women's Health 2011;20(10):1525–1528; Laurikainen E, et al., Five-year Results of a Randomized Trial Comparing Retropubic and Transobturator Midurethral Slings for Stress Incontinence. Eur Urol 2014 Jun;65(6):1109–14; Athanasiou S, et al., Seven years of objective and subjective outcomes of transobturator (TVT-O) vaginal tape: Why do tapes fail? 2014;25:219–225; Serati M, et al., TVT-O for the Treatment of Pure Urodynamic Stress Incontinence: Efficacy, Adverse Effects, and Prognostic Factors at 5-Year Follow-up. Eur Urol 2013;63:872–78; Liapis A, et al., Efficacy of inside-out transobturator vaginal tape (TVTO) at 4 years follow up. 2010;148:199–201; Angioli R, et al., Tension-Free Vaginal Tape Versus Transobturator Suburethral Tape: Five-Year Follow-up Results of a Prospective, Randomised Trial. Eur Urol 2010;58:671–677; Cheng D, et al., Tension-free vaginal tape-obturator in the treatment of stress urinary incontinence: a prospective study with five-year follow-up. Eur J Obstet Gynecol Reprod Biol 2012;161:228–231.)

A recent high-quality Cochrane meta-analysis review of the literature concludes that TVT, TVT-O, and Burch procedures have similar efficacy, but the TVT and TVT-O procedures involve shorter recovery time. The review further concludes that midurethral synthetic sling operations are the most extensively researched surgical treatment for SUI in women and have a good safety profile. The TVT, in particular, is the most studied mesh device, with more than 100 randomized controlled trials having been done with the device. The Cochrane review authors note that irrespective of the routes traversed, synthetic mesh midurethral slings are highly effective in the short and medium term, and evidence demonstrates their effectiveness in the long-term. The Cochrane Review illustrates positive impact on improving the quality of life of women with SUI. With the exception of groin pain, fewer adverse events occur with employment of a transobturator approach. (Ford AA, Rogerson L, Cody JD, Ogah J. Mid-urethral sling operations for stress urinary incontinence in women. Cochrane Database of Systematic Reviews 2015, Issue 7. Art. No.: CD006375. DOI:

10.1002/14651858.CD006375.pub3.) The 2015 Cochrane systematic review demonstrates that both retropubic and transobturator approaches appear to be comparable in terms of efficacy and patient satisfaction. (ACOG / AUGS Practice Bulletin No. 155; Nov. 2015.) However, a 2015 systematic review and meta-analysis observed similar rates of objective cure between transobturator and retropubic midurethral slings, and higher subjective cure rates in retropubic slings. (Tommaselli GA, et al., Medium-term and long-term outcomes following placement of midurethral slings for stress urinary incontinence: a systematic review and metaanalysis. Int Urogynecol J 2015.)

In 2010, Novara added 14 new trials to their 2007 systematic review metaanalysis evaluating efficacy, complication rate, and reoperation rate of Burch colposuspension and synthetic midurethral slings. Midurethral slings were found to have higher objective cure rates than Burch colposuspension. Similar rates of postoperative complications, including pelvic hematoma, UTI, postoperative lower urinary tract symptoms, and reoperation were noted between the two groups. Midurethral slings resulted in a greater improvement in patient quality of life over the Burch procedure in two trials. Midurethral slings were also found to be more cost-effective than the Burch procedure. (Cox A, Herschorn S, Lee L, Surgical management of female SUI: is there a gold standard? Nature 2013;10:78-89.) Based on the literature, a new gold standard for first-line surgical treatment for women with SUI has emerged—the synthetic midurethral sling inserted via retropubic or transobturator approach. (Cox A, Herschorn S, Lee L, Surgical management of female SUI: is there a gold standard? Nature 2013;10:78-89.) Studies have shown that midurethral slings are superior to both the Burch procedure and pubovaginal slings in terms of cure rates. (Schimpf MO, et al., Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. Am J Obstet Gynecol 2014;210:1.e1-1.e27.) Objective cure rate at one year is greater than 90%, and 85% at seventeen years. (Nilsson CG, et al., Seventeen years' follow-up of the tension-free vaginal tape procedure for female stress urinary incontinence. Int Urogynecol J 2013 Aug;24(8):1265–1269.)

Due to the increased morbidity of the open Burch procedure, it is less frequently taught in residencies and fellowships. Almost all residents, however, are trained on midurethral slings as the primary treatment option for SUI management. The TVT retropubic and transobturator approaches are commonly taught and performed in training programs throughout the world.

The TVT and TVT-O have proven long-term efficacy due to the permanence and stability of the mesh and are superior in efficacy to retropubic suspensions. (Aigmueller T, et al., Ten-year follow-up after the tension-free vaginal tape procedure. Am J Obstet Gynecol 2011 Nov;205(5):496.e1–5.) Compared with open or laparoscopic colposuspension the success rates are more stable with a lesser decline of success over years. Reported long-term success rates after open or laparoscopic colposuspension vary between 36% and 69%. (Alcalay M, et al., Burch colposuspension: a 10-20 year follow up. Br J Obstet Gynaecol 1995;102:740-745; Barr S. The long-term outcome of laparoscopic colposuspension: a 10-year cohort study. Int. Urogynecol J 2009:20:443-5.)

I have personally performed over 1,000 TVT procedures, including the TVT, the TVT-O and the more recent TVT-Exact and TVT-Abbrevo, and have found the products to be safe and efficacious when following the appropriate patient selection and the technique described by Drs.

Ulmsten and de Leval, which is covered in the product instructions for use. I have lectured and proctored physicians on the safe use of the TVT, TVT-O, and several other devices since 2000. The devices are high quality, straightforward, and the polypropylene mesh is stable over time, as I have patients implanted 15 years ago and see no long-term complication trends. Since the television advertisements claiming pelvic mesh is a dangerous product, I have received hundreds of phone calls from anxious patients with fears of product recalls and future complications. The overwhelming majority of those anxious patients have excellent outcomes and no adverse symptoms. The effect on current patients is to create fear that a synthetic sling will cause future problems and many choose not to proceed to treatment. There is a 30% reduction in the number of patients undergoing stress incontinence and pelvic reconstructive surgery. (Perkins CE, Warrior K, Eilber KS, et al. The Role of Mid-urethral Slings in 2014: Analysis of the Impact of Litigation on Practice. Curr Bladder Dysfunct Rep (2015) 10:39-45. DOI 10.1007/s11884-014-0278-z; Koo K, Gormley EA, Abstract MP81-05: Transvaginal Mesh in the Media Following the 2011 FDA Update.)

The efficacy and safety of the TVT and TVT-O are well-reported. The TVT is the most studied midurethral sling, with more than 100 RCTs. The TVT-O has also been extensively studied—with thousands of patients included in the collection of studies. Additionally, the following professional organization position statements and guidelines and FDA publications have addressed the safety, efficacy, and widespread acceptance of synthetic mesh midurethral slings like the TVT and TVT-O.

- **ACOG / AUGS Practice Bulletin No. 155; Nov. 2015.**
  - "Synthetic midurethral mesh slings are the most common primary surgical treatment for stress urinary incontinence in women. Synthetic midurethral slings demonstrate efficacy that is similar to traditional suburethral fascial slings, open colposuspension, and laparoscopic colposuspension. Compared with suburethral fascial slings, fewer adverse events have been reported with synthetic midurethral slings. Voiding dysfunction is more common with open colposuspension than with synthetic midurethral slings. For these reasons, midurethral synthetic mesh slings have become the primary surgical treatment for stress urinary incontinence in women."
  - "Although controversy exists about the role of synthetic mesh used in the vaginal repair of pelvic organ prolapse, there are substantial safety and efficacy data that support the role of synthetic mesh midurethral slings as a primary surgical treatment option for stress urinary incontinence in women. For this reason, and to clarify uncertainty for patients and practitioners, the American Urogynecologic Society and the Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction published a position statement recognizing polypropylene mesh midurethral slings as the 'standard of care' in the surgical treatment of stress urinary incontinence."
- **AUGS-SUFU, Position Statement on Mesh Midurethral Slings for Stress Urinary Incontinence (Jan. 3, 2014)**
  - "The polypropylene mesh midurethral sling is the recognized worldwide standard of care for the surgical treatment of stress urinary incontinence.

The procedure is safe, effective, and has improved the quality of life for millions of women."

- "Polypropylene material is safe and effective as a surgical implant. Polypropylene has been used in most surgical specialties (including general surgery, cardiovascular surgery, transplant surgery, ophthalmology, otolaryngology, gynecology, and urology) for over five decades."
- "As a knitted implant for the surgical treatment of SUI, macroporous, monofilament, light weight polypropylene has demonstrated long term durability, safety, and efficacy up to 17 years."
- "The monofilament polypropylene mesh MUS is the most extensively studied anti-incontinence procedure in history. A broad evidence base including high quality scientific papers in medical journals in the US and the world supports the use of the MUS as a treatment for SUI. There are greater than 2000 publications in the scientific literature describing the MUS in the treatment of SUI. These studies include the highest level of scientific evidence in the peer reviewed scientific literature. . . . No other surgical treatment for SUI before or since has been subject to such extensive investigation."
- "Polypropylene mesh midurethral slings are the standard of care for the surgical treatment of SUI and represent a great advance in the treatment of this condition for our patients. Since the publication of numerous level one randomized comparative trials, the MUS has become the most common surgical procedure for the treatment of SUI in the US and the developed world. This procedure has essentially replaced open and transvaginal suspension surgeries for uncomplicated SUI. . . . Full-length midurethral slings, both retropubic and transobturator, have been extensively studied, are safe and effective relative to other treatment options and remain the leading treatment option and current gold standard for stress incontinence surgery. Over 3 million MUS have been placed worldwide and a recent survey indicates that these procedures are used by >99% of AUGS members."
- "The polypropylene midurethral sling has helped millions of women with SUI regain control of their lives by undergoing a simple outpatient procedure that allows them to return to daily life very quickly. With its acknowledged safety and efficacy it has created an environment for a much larger number of women to have access to treatment. In the past, concerns over failure and invasiveness of surgery caused a substantial percent of incontinent women to live without treatment. One of the unintended consequences of this polypropylene mesh controversy has been to keep women from receiving any treatment for SUI. This procedure is probably the most important advancement in the treatment of stress urinary incontinence in the last 50 years and has the full support of our organizations which are dedicated to improving the lives of women with urinary incontinence."

- **AUGS Position Statement on Restriction of Surgical Options for Pelvic Floor Disorders (2013)**
  - "The American Urogynecologic Society strongly opposes any restrictions by state or local medical organizations, healthcare systems, or insurance companies which ban currently available surgical options performed by qualified and credentialed surgeons on appropriately informed patients with pelvic floor disorders."
  - "In a recent study involving 53 expert urologists and urogynecologists (of whom >90% were fellowship trained) and who could select among many surgical options, the full-length synthetic midurethral sling was the preferred option in 93% for the surgical treatment of primary stress incontinence. Full-length midurethral slings, both retropubic and transobturator, have been extensively studied, are safe and effective relative to other treatment options and remain the leading treatment option and current gold standard of care for stress incontinence surgery."
- **AUA Position Statement on the Use of Vaginal Mesh for the Surgical Treatment of Stress Urinary Incontinence (Nov. 2011).**
  - "Suburethral synthetic polypropylene mesh sling placement is the most common surgery currently performed for SUI. Extensive data exist to support the use of synthetic polypropylene mesh suburethral slings for the treatment of female SUI, with minimal morbidity compared with alternative surgeries. Advantages include shorter operative time/anesthetic need, reduced surgical pain, reduced hospitalization, and reduced voiding dysfunction. Mesh-related complications can occur following polypropylene sling placement, but the rate of these complications is acceptably low."
  - "Multiple case series and randomized controlled trials attest to the efficacy of synthetic polypropylene mesh slings at 5-10 years. This efficacy is equivalent or superior to other surgical techniques. There is no significant increase in adverse events observed over this period of follow-up. Based on these data, the AUA Guideline for the Surgical Management of Stress Urinary Incontinence (2009) concluded that synthetic slings are an appropriate treatment choice for women with stress incontinence, with similar efficacy but less morbidity than conventional non-mesh sling techniques."
- **IUGA – Stress Urinary Incontinence – A Guide for Women (2011)**
  - "Before 1993, the treatment of stress incontinence often involved major surgery with an abdominal incision. The most common treatment now involves the use of a permanent sling that lies under the middle section of the urethra."
- **ICS Fact Sheets: A Background to Urinary and Faecal Incontinence (July 2013)**
  - "Worldwide, midurethral slings comprised of synthetic mesh have become the treatment of choice for SUI. Long-term data are robust and demonstrate durable efficacy with a very low complication rate, particularly in experienced hands. Various techniques for sling placement

and different meshes are employed according to physician preference, but all appear to be equally effective.

- **Lucas MG, Ruud JLB, Burkhard FC, et al., EAU Guidelines on Surgical Treatment of Urinary Incontinence. European Urol 62 (2012) 1118-1129.**
  - "There has been a rapid adoption of midurethral synthetic sling insertion as the first-line surgical option for SUI because it is effective, it is less invasive, and patients recover more quickly. "
  - Notes that a systematic review of midurethral slings with both open colposuspension and laparoscopic colposuspension showed that retropubic insertion of a synthetic midurethral sling gave equivalent patient-reported and superior clinician-reported cure of SUI compared with colposuspension at 12 months; transobturator insertion gave equivalent patient-reported and clinician-reported cure of SUI at 12 months. Also notes that midurethral sling insertion was associated with a lower rate of new symptoms of urgency and voiding dysfunction compared with colposuspension.
- **NICE clinical guideline 171. Urinary incontinence: The management of urinary incontinence in women. (Sept. 2013).**
  - Notes that if conservative management for SUI has failed, the surgeon should offer, among other options, a synthetic mid-urethral tape.
  - Notes that, when offering a synthetic mid-urethral tape procedure, surgeons should use procedures and devices for which there is current high quality evidence of efficacy and safety. Footnote 11 then notes that at the time of publication, TVT and TVT-O (among others) met this guideline.
- **FDA, Considerations about Surgical Mesh for SUI (2013)**
  - "Mesh sling procedures are currently the most common type of surgery performed to correct SUI. Based on industry estimates, there were approximately 250,000 of these procedures performed in 2010."
  - "The safety and effectiveness of multi-incision slings is well-established in clinical trials that followed patients for up to one-year. Longer follow-up data is available in the literature, but there are fewer of these long-term studies compared to studies with one-year follow-up."
- **FDA Executive Summary, Surgical Mesh for Treatment of Women with Pelvic Organ Prolapse and Stress Urinary Incontinence (Sept. 8-9, 2011)**
  - Notes that the Burch has a long history, but its popularity has declined over the past two decades with the introduction of less invasive procedures. Notes that pubovaginal sling procedures using biologic graft material (often autologous fascia) similarly have declined in popularity.
  - Notes that anterior repair with Kelly plication to correct SUI in the presence of a cystocele and bladder neck needle suspension is rarely performed currently due to poor long-term outcomes.
  - "A substantial number of quality clinical trials, as well as systematic reviews, have been published for the first generation minimally invasive slings that provide evidence of safety and effectiveness of these devices." (p. 28)

- "After considering all available data on both safety and effectiveness, and considering the risk/benefit profile, it appears that new premarket clinical trials are not warranted for minimally invasive slings for SUI unless the device has new features (*e.g.* new polymer or coating) that could affect device performance."

- **FDA 24-hr Summary – Ob/Gyn Devices Panel (Sept. 8-9, 2011)**
  - Notes that the panel consensus on retropubic and transobturator suburethral slings was that the safety and effectiveness of these devices is well-established."
- **Dmochowski RR, Blaivas JM, Gormley EA, et al., Update of AUA Guideline on the Surgical Management of Female Stress Urinary Incontinence. J. Urol. 183: 1906-1914 (May 2010).**
  - Noting the importance of the transobturator technique in the treatment of SUI and that midurethral slings are one treatment modality that may be considered for the index patient.
- **AUA Position Statement on the Use of Vaginal Mesh for the Surgical Treatment of Stress Urinary Incontinence (2012)**
  - "Suburethral synthetic polypropylene mesh sling placement is the most common surgery currently performed for SUI. Extensive data exist to support the use of synthetic polypropylene mesh suburethral slings for the treatment of female SUI, with minimal morbidity compared with alternative surgeries. Advantages include shorter operative time/anesthetic need, reduced surgical pain, reduced hospitalization, and reduced voiding dysfunction. Mesh-related complications can occur following polypropylene sling placement, but the rate of these complications is acceptably low. Furthermore, it is important to recognize that many sling-related complications are not unique to mesh surgeries and are known to occur with non-mesh sling procedures as well. It is the AUA's opinion that any restriction of the use of synthetic polypropylene mesh suburethral slings would be a disservice to women who choose surgical correction of SUI."
  - "Multiple case series and randomized controlled trials attest to the efficacy of synthetic polypropylene mesh slings at 5–10 years. This efficacy is equivalent or superior to other surgical techniques. There is no significant increase in adverse events observed over this period of follow-up. Based on these data, the AUA Guideline for the Surgical Management of Stress Urinary Incontinence (2009) concluded that synthetic slings are an appropriate treatment choice for women with stress incontinence, with similar efficacy but less morbidity than conventional non-mesh sling techniques."

Plaintiffs' experts' theory of mesh degradation is not substantiated in the literature or in my personal experience using polypropylene slings and mesh for incontinence treatment and pelvic reconstruction. Studies of explanted mesh are difficult to interpret, as there is damage to the material during explantation, treatment with chemicals to remove the collagen and biologic matrix that has incorporated into the mesh, and preparation onto slides for microscopic

examination. There is no literature to support clinically significant mesh degradation in humans. Polypropylene suture is used by vascular surgeons on major blood vessels and in my practice when tying off renal arteries and repairing the largest vein in the body; the vena cava. If there was a question of degradation or loss of strength over time, Prolene suture would not be the suture of choice for the highest-risk surgery. The studies often relied on by plaintiffs' experts offering the opinion that the Prolene mesh degrades are unreliable and do not support that theory. For instance, the Clavé study from 2010 is unreliable and does not show degradation. The chemical analyses performed on a limited subset of the specimens does not show degradation, and the scanning electron microscope photos in the study show surface cracking that could be from biologic material and handling or preservation rather than the cracking of the polypropylene itself. Also, the sample analyzed in the study was only 32 out of the 100 specimens, and the authors fail to discuss how those 32 specimens were selected. They also fail to discuss whether the mesh was damaged during surgical explantation.

Nor have I seen a problem with Prolene mesh roping or curling, unless it is placed improperly by over-tensioning. Nor have I observed particle loss from mechanically cut mesh in my practice. Even if there was particle loss from the mechanically cut Prolene mesh, the particles lost would be the same Prolene as the suture material that is FDA approved as safe and effective for use in the human body. Furthermore, the mesh does not contract or experience pore collapse when placed according to the IFU. The sheath that covers the mesh on the TVT and TVT-O devices protects the tissue against trauma, helps the mesh pass through the tissue smoothly, and carries the forces of implantation so that the mesh retains its shape. Scar tissue that forms after any pelvic surgery contracts, and tissue incorporating into implanted mesh is no exception, but the mesh itself does not contract. (Nilsson, CG, Seventeen years' follow-up of the tension-free vaginal tape procedure for female stress urinary incontinence. Int Urogynecol J 2013 Aug;24(8):1265–1269; Lukacz ES, et al., The effects of the tension-free vaginal tape on proximal urethral position: a prospective, longitudinal evaluation. Int Urogynecol J 2004 Jan-Feb;15(1):32-38.)

There is no practical or clinical difference between mechanically cut or laser-cut mesh in terms of how it is deployed or incorporated in the tissues. (ETH.MESH.01784823-28 (CER Laser Cut Mesh); ETH.MESH.01222075-79 (Elongation Characteristics of Laser Cut Prolene Mesh for TVT); ETH.MESH.06696367-79 (Performance Evaluation of TVT U Prolene Mesh); Lin AT, et al., In Vivo tension Sustained by Fascial Sling in Pubovaginal Sling Surgery for Female Stress Urinary Incontinence, J Urol , 2005 Mar;173(3):894–897.) Mesh is not pre-stretched to 50% elongation before it is used, and it is implanted with trocars and with a protective sheath over the mesh. The mesh sling must be stiff enough to lie flat against the posterior urethra with porosity large enough to encourage fibroblast and collagen deposition for incorporation, and it must have enough elasticity to allow give during dynamic stressing that occurs with activity. Mesh requires an optimal level of stiffness to properly do its job supporting the urethra. Based on my experience and my assessment of the available literature, I do not believe that any particle loss from mechanically cut Prolene polypropylene mesh has a clinical effect in patients. Both laser-cut and mechanically cut Prolene mesh is safe and efficacious as demonstrated by the medical literature and in my experience.

Plaintiffs' experts assert that the Prolene mesh used in the TVT and TVT-O is small-pore mesh. That is not true. The Ethicon TVT mesh has the largest porosity, and greatest elasticity of all the SUI meshes available. It is also monofilament and knitted to provide the optimal combination of biocompatibility and minimal inflammatory response. The mesh—which has a pore size of approximately 1,379 microns—allows adequate tissue incorporation/ingrowth. (Amid PK, Classification of biomaterials and their related complications in abdominal wall hernia surgery. Hernia 1997;1:15–21.) The Ethicon mesh is not associated with an increased risk of infection compared to other SUI vaginal surgeries. Verified infection after TVT or TVT-O is a very rare occurrence, and has not occurred in my practice in over 1,000 cases and 15 years.

Nor is the TVT or TVT-O mesh "heavyweight" mesh. Synthetic slings require an optimal amount of weight/density to properly do their job supporting the urethra without adversely affecting its function. Indeed, seventeen-year follow-up substantiates the biocompatibility of the weight/stiffness/elasticity and porosity of the TVT mesh. At seventeen years of follow-up, 91.3% of patients' SUI was objectively cured, and there was no tape rejection, no clinically significant contracture, and only one mesh exposure, which was not symptomatic and was due to vaginal atrophy in an elderly patient. (Nilsson, CG, Seventeen years' follow-up of the tension-free vaginal tape procedure for female stress urinary incontinence. Int Urogynecol J 2013 Aug;24(8):1265–1269.)

Plaintiffs' experts have also claimed that the mesh used in the TVT and TVT-O devices is cytotoxic and causes an excessive inflammatory response. This is not supported in the literature, and I have not seen it in my practice. The long-term studies on the TVT and TVT-O mesh belie this claim. Studies show minimal inflammation associated with the Prolene mesh used in TVT and TVT-O, and practically no tissue reaction out to two years. (Falconer C, et al. Influence of different sling materials on connective tissue metabolism in stress urinary incontinent women. Int Urogynecol J Pelvic Floor Dysfunct. 2001;12 Suppl 2:S19-23.) The mere presence of chronic inflammatory cells in a tissue specimen does not prove that there is a chronic inflammatory process that is active. Such cells can be present but quiescent, and can be seen in vaginal tissue even when no mesh or other foreign body has been implanted. If it were the case that the mesh in the TVT and TVT-O devices was cytotoxic, the many intermediate- and long-term studies on the products would not demonstrate the high efficacy and low complication rates that they do.

Any suggestion by plaintiffs' experts that PVDF is a safer alternative to the Prolene mesh used in the TVT and TVT-O devices is untenable. There is no mid- or long-term data supporting the use of PVDF in SUI treatment. To my knowledge, PFDF has not been studied to treat SUI in women. Plaintiffs' experts may also claim that Ultrapro or Vypro mesh would have been a safer alternative to the Prolene mesh used in the TVT and TVT-O slings. However, with respect to Vypro, a study of the use of that mesh in pelvic floor surgery showed that tolerance of the Vypro mesh was "very poor" and associated with high rates of erosion and cicatrisation. (Denis S, et al., Pelvic Organ Prolapse Treatment by the Vaginal Route Using a Vypro Composite Mesh: Preliminary Results About 106 Cases. ICS IUGA 2004; Abstract 620.) With respect to Ultrapro, the study often cited by plaintiffs' experts in support of that material as a safer alternative to the Prolene TVT mesh is the Okulu study, but that study does not compare TVT mesh to Ultrapro mesh, and involves a technique completely different than the one used to implant the TVT or

TVT-O slings. (Okulu E, et al., Use of three types of synthetic mesh material in sling surgery: A prospective randomized clinical trial evaluating effectiveness and complications. Sand J Urol 2013;47:217–224.) Ethicon studied the use of Ultrapro mesh with a sheath and found that the force required to remove the sheath was excessive, which it believed to be due to the fact that the mesh stuck to the sheath after sterilization. (R&D Memorandum on PA Mesh Assessments for TVTO-PA, ETH.MESH.09922570.)

Plaintiffs' experts sometimes suggest or claim that the Prolene mesh is carcinogenic, but there is no reliable scientific evidence to support the theory or claim that polypropylene can cause cancer or sarcoma. In the more than 1,000 cases in which I have implanted one of the TVT family of products, I have not seen a single case of cancer attributable to the mesh. The literature also refutes plaintiffs' experts' suggestion or claim. (King AB, et al. Is there an association between polypropylene midurethral slings and malignancy? Urology. 2014 Oct;84(4):789-92; King AB, Goldman HB. Current controversies regarding oncologic risk associated with polypropylene midurethral slings. Curr Urol Rep. 2014 Nov;15(11):453; Linder BJ, et al., Evaluation of the local carcinogenic potential of mesh used in the treatment of female stress urinary incontinence. Int Urogynecol J 2016. DOI 10.1007/s00192-016-2961-4.) The medical literature contains no case reports of tumors caused by or associated with polypropylene implantation despite the fact that polypropylene has been implanted in millions of people. (AUGS & SUFU, Frequently Asked Questions by Providers—Mid-urethral Slings for Stress Urinary Incontinence (available at http://www.augs.org/p/bl/et/blogaid=194).)

The mesh used in the TVT and TVT-O slings is the most commonly used mesh for treatment of stress urinary incontinence and is state of the art. Many long- and intermediate-term studies consistently show that the TVT and TVT-O are safe and effective and the standard of care for surgical treatment of SUI. (Serati M, et al., TVT for the Treatment of Urodynamic Stress Incontinence: Efficacy and Adverse Effects at 13-Year Follow-Up. Neurourol and Urodynamics DOI 10.1002/nau; Groutz A, et al., Long-Term Outcome of Transobturator Tension-Free Vaginal Tape: Efficacy and Risk Factors for Surgical Failure. J of Women's Health 2011;20(10):1525–1528; Laurikainen E, et al., Five-year Results of a Randomized Trial Comparing Retropubic and Transobturator Midurethral Slings for Stress Incontinence. Eur Urol 2014 Jun;65(6):1109–14; Athanasiou S, et al., Seven years of objective and subjective outcomes of transobturator (TVT-O) vaginal tape: Why do tapes fail? 2014;25:219–225; Serati M, et al., TVT-O for the Treatment of Pure Urodynamic Stress Incontinence: Efficacy, Adverse Effects, and Prognostic Factors at 5-Year Follow-up. Eur Urol 2013;63:872–78; Liapis A, et al., Efficacy of inside-out transobturator vaginal tape (TVTO) at 4 years follow up. 2010;148:199–201; Angioli R, et al., Tension-Free Vaginal Tape Versus Transobturator Suburethral Tape: Five-Year Follow-up Results of a Prospective, Randomised Trial. Eur Urol 2010;58:671–677; Cheng D, et al., Tension-free vaginal tape-obturator in the treatment of stress urinary incontinence: a prospective study with five-year follow-up. Eur J Obstet Gynecol Reprod Biol 2012;161:228–231; Heinonen P, et al., Tension-free vaginal tape procedure without preoperative urodynamic examination: long-term outcome. Int J Urol. 2012 Nov;19(11):1003-9; Aigmueller T, et al., Ten-year follow-up after the tension-free vaginal tape procedure. Am J Obstet Gynecol 2011 Nov;205(5):496.e1-5; Olsson I, et al., Long-term efficacy of the tension-free vaginal tape procedure for the treatment of urinary incontinence: a retrospective follow-up 11.5 years post-operatively. Int Urogynecol J 2010 Jun;21(6):679–683; Liapis A, et al., Long-term efficacy of

tension-free vaginal tape in the management of stress urinary incontinence in women: efficacy at 5- and 7-year follow-up. Int Urogynecol J 2008 Nov;19(11):1509-1512; Svenningsen R, et al., Long-term follow-up of the retropubic tension-free vaginal tape procedure. Int Urogynecol J. 2013 Aug;24(8):1271-8; Chêne G, et al., Long-term results of tension-free vaginal tape (TVT) for the treatment of female urinary stress incontinence. Eur J Obstet Gynecol Reprod Biol 2007 Sep;134(1):87-94; Vesna Bjelic-Radisic V, Patient-related Outcomes and Urinary Continence Five Years After the Tension-Free Vaginal Tape Operation, Neurourology and Urodynamics 2011;30(8):1512-1517 (2011); Jin-Yan Wu JY, et al., Surgical therapies of female stress urinary incontinence: experience in 228 cases, Int Urogynecol J 2010 Jun;21(6):645-649; Song PH, et al., The 7-year outcome of the tension-free vaginal tape procedure for treating female stress urinary incontinence. BJU Int 2009 Oct;104(8):1113-1117; Kuuva N, et al., Long-term results of the tension-free vaginal tape operation in an unselected group of 129 stress incontinent women. Acta Obstet Gynecol 2006;85(4):482-487; Celebi I, et al., Results of the tension-free vaginal tape procedure for treatment of female stress urinary incontinence: a 5 year follow-up. Arch Gynecol Obstet 2009 Apr;279(4):463-467; Prien-Larsen JC, et al., Long-term outcomes of TVT and IVS operations for treatment of female stress urinary incontinence: monofilament vs. multifilament polypropylene tape. Int Urogynecol J 2009 Jun;20(6):703-709; Jelovsek JE, et al, Randomized trial of laparoscopic Burch colposuspension versus tension-free vaginal tape: long-term follow up. BJOG 2008 Jan;115(2):219-225; McCracken GR, et al., Five Year Follow-up Comparing Tension-Free Vaginal Tape and Colposuspension, Ulster Med J 2007 Sep;76(3):146-149.)

The incidence of mesh exposure is low, but varies in studies between 1 and 5%. A short version Cochrane Review in 2011 observed that the monofilament synthetic mid-urethral slings—such as the TVT and TVT-O—were more efficacious and were associated with a lower rate of erosion than multifilament non-type-1 meshes. (Ogah J, Cody DJ, Rogerson L. Minimally invasive synthetic suburethral sling operations for stress urinary incontinence in women: a short version Cochrane review. Neurourol Urodyn. 2011 Mar;30(3):284-91.) Mesh exposure is usually asymptomatic, can cause a vaginal discharge and possibly cause coital discomfort in the male partner. Management can be topical application of vaginal estrogen or excision under local anesthetic in the office. Removal of the exposed mesh can still provide continence 80-90% of the time. (Klutke C, et al., Urinary retention after tension-free vaginal tape procedure: incidence and treatment. Urology 2001 Nov;58(5):697-701.) While mesh-related complications can occur after placement of a polypropylene sling, the rate of such complications is acceptably low. The rate of reoperation has consistently reported to be approximately 2–5% for voiding dysfunction and exposure after a decade or more of follow-up in various studies, meta-analyses, and database reviews. (Welk B, et al., Removal or Revision of Vaginal Mesh Used for the Treatment of Stress Urinary Incontinence. JAMA Surg 2015 Sep;9:1–9; Unger CA, et al., Indications and risk factors for midurethral sling revision. Int Urogynecol J 2015 Jul 2; Schimpf MO, et al., Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. Am J Obstet Gynecol 2014;210:1.e1-1.e27; Laurikainen E, et al., Five-year Results of a Randomized Trial Comparing Retropubic and Transobturator Midurethral Slings for Stress Incontinence. Eur Urol 2014 Jun;65(6):1109–14; Jonsson Funk M, et al., Sling revision/removal for mesh erosion and urinary retention: long-term risk and predictors. Am J Obstet Gynecol 2013 Jan;208(1):73.e1–7; Svenningsen R, et al., Long-term follow-up of the retropubic tension-free vaginal tape procedure. Int Urogynecol J. 2013 Aug;24(8):1271-8; Nguyen JN, et al., Perioperative complications and reoperations after

incontinence and prolapse surgeries using prosthetic implants. Obstet Gynecol 2012 Mar; 119(3):539–546; Ogah, J., Cody, JD, Rogerson, L., Minimally invasive synthetic suburethral sling operations for stress urinary incontinence in women. Cochrane Database of Systematic Reviews 2009, Issue 4. Art. No.: CD006375. DOI:10.1002/14651858.CD006375.pub2; Novara G, et al., Complication Rates of Tension-Free Midurethral Slings in the Treatment of Female Stress Urinary Incontinence: A Systematic Review and Meta-Analysis of Randomized Controlled Trials Comparing Tension-Free Midurethral Tapes to Other Surgical Procedures and Different Devices. Eur Urol 2008 Feb;53(2):288–309.)

V. The TVT and TVT-O's Instructions for Use and Other Educational Materials

a. Ethicon's Instructions for Use

The instructions for use (IFU) included with the devices are specific in detail to allow the safe deployment of the devices. The procedures are adequately described such that a trained and experienced physician could implant the devices safely and effectively. The indications are adequately described in terms of patient selection and contraindications for surgery. The contraindications and warnings are adequately described based on my experience and review of the literature. The IFU is not intended to teach surgical technique, which is assumed to have been in the skill set of the surgeon. Every pelvic surgeon should be aware of the intraoperative and post-operative risks inherent. A surgeon need not be taught the entire practice of medicine in an IFU. The totality of surgical risks of pelvic floor surgeries is not included in the IFU for gynecologists or urologists. Surgeons have training from numerous sources—medical school, residency, maybe fellowships, colleagues' experiences, their own experience, literature, etc. The IFU is used by the surgeon to become familiar with the specific device, the handling, placement and deployment in the manner that maximizes safety and efficacy. The IFU is never assumed to be a completely comprehensive list of all the possible adverse complications that are low prevalence. The IFU is intended to guide the surgeon to perform the procedure as the device was designed.

Mesh exposure and erosion are the only unique risks to mesh surgeries, and are essentially wound complications. Wound complications can also occur with other surgeries. Mesh exposure can be caused by poor quality tissue due to atrophic vaginitis, history of pelvic radiation therapy, too superficial dissection prior to sling placement, hematoma, and early sexual activity. The IFU advises surgeons that:

- Failure to follow instructions may result in improper functioning of the device and lead to injury.
- It's not a comprehensive reference to surgical technique for treating SUI.
- The device should only be used by physicians trained in the surgical treatment of SUI and specifically in implanting the TVT device.
- All information should be reviewed prior to performing this procedure.

The IFU package insert is included with each device and is used as a guide for the surgeon to use the device in the manner it is intended. The IFU lists indications for use, contraindications, most prevalent risks, and the detailed description of how to deploy the device

safely. IFUs in general are not intended to list every possible adverse event or post-operative complication. The IFU is generally understood to be a guide in the proper deployment of the device. Surgeons are trained in residency how to manage vaginal surgery with anatomy, handling of tissues, defining surgical planes, and perioperative care. The IFU functions to describe how this particular device is best deployed but the patient selection, preoperative informed consent, perioperative management, and post-operative care of the patient is the surgeon's responsibility. The patient's degree of severity of vaginal prolapse and stress incontinence, with consideration of patient age, tissue integrity, previous pelvic surgery, health status, tobacco usage, and steroid or opioid dependency leads the surgeon to make a complex decision about surgical approach and the likelihood of success.

b. Ethicon's Training Programs

Ethicon began offering didactic training programs for the TVT in 1999 and later for pelvic prolapse repair when both Gynemesh and Prolift became available. The programs include didactic lectures followed by hands-on cadaver labs with experienced pelvic surgeons at each cadaver station guiding the use of the devices with step-by-step instructions about the use of the products. The didactic lectures are provided by faculty members invited from academia and private practice with extensive backgrounds in pelvic surgery and the use of Ethicon products. The programs include discussions about disease state, indications for surgery, contraindications, avoidance of complications, and the safe use of the products. Every course included a discussion of management of complications and questions from the audience. Webinars, and telesurgery programs were also offered for surgeons that previously attended cadaver labs, or were for advanced users to become familiar with the newer devices, and for dissemination of information on longer-term results when new papers were published. The preceptors are independent of Ethicon, are required to teach the courses in compliance with the slide set provided so as not to advocate or discuss any off-label uses of the products. I began as a preceptor in 2000 with the TVT and later TVT-O, TVT-Abbrevo, TVT-Secur, Prolift, and Prosima devices. I was thoroughly familiar with the products having performed the surgeries in my own practice. Contributing as a preceptor is professionally fulfilling, as it requires that I remain current in the field, and have the opportunity to collaborate with experts both nationally and internationally. There is a lack of opportunity for surgeons to learn and train on new technologies outside of residency, and Ethicon provided resources that are much appreciated by those pelvic surgeons who would like to stay current and improve their patient outcomes. Each course collected anonymous questionnaires and feedback from the attendees rating the quality of the course and proctors, including whether they felt there was commercial bias. Overwhelmingly, the response was positive, and those proctors that were not received well were disinvited to teach future courses. The faculty has the opportunity to discuss surgical techniques and management of possible complications prior to each course.

Even after a surgeon attends a course, no certification can be provided that will ensure credentialing at their respective hospitals. Each hospital has a surgery committee that reports to the credentials committee that grants privileges for specific procedures. Surgeons must demonstrate previous training through residency, and the quality assurance department will track patient outcomes and complications. Hospitals vary in their requirements for credentialing, which includes proctoring and/or close surveillance of outcomes for new technologies or

procedures. The medical device industry can provide education and training, but does not grant privileges for the use of their products. Surgeons are granted privileges based on the background training, residency director recommendations, and review of malpractice history and National Data Bank files. When credentials committees grant privileges for a specific area, they will not state specific proprietary procedures, but rather generalized areas such as cystourethropexies rather than MMK procedures or the Burch procedure.

c. Ethicon's Patient Brochures

Ethicon's Patient brochures provide information about the medical condition of incontinence, the different types, and treatment options ranging from behavior modification with pelvic exercises, electrical stimulation, medications, and bulking agents, to surgery. The information provided gives general terminology of the disease state, possible causes, and symptoms, as well as diagnosis and treatment options. The brochures are not intended to be in-depth and comprehensive, but rather to serve as a reference along with the website to pursue further information if desired. A list of contraindications for surgery is also included. The description of the procedure includes the most frequently encountered possible adverse events and repair options. The brochures are not intended and have never been used in my practice to serve as the only source of preoperative informed consent. Patients are separately informed about the indications, alternative treatments, and description of how the mesh sling will be implanted. Risks of bleeding, infection, bowel or bladder injury, persistent incontinence, retention, and pain are discussed. The possibility of mesh exposure or erosion is also discussed with re-operative repair techniques or application of vaginal cream. The information clearly states to discuss any questions with the surgeon and also provides a toll-free number to call to discuss questions with an on-call nurse.

VI. The Design of the TVT and TVT-O Devices

a. The Usefulness, Desirability, and Safety of the Devices

Prior to the availability of the TVT and TVT-O in the U.S., surgery for stress incontinence had been more morbid and less predictable in surgical treatment outcomes. Patients who have undergone open suspensions such as a Burch procedure that have failed are reluctant to undergo reoperation due to the long and painful recovery from the open repair. Surgeries that attempt to pull up and fix the urethra and bladder neck to the pubic bone require a more extensive surgical dissection, which increases blood loss, operative time, require larger incisions, and could cause damage to the neurovascular support of the bladder neck and urethra. Suspending procedures such as the Stamey, Peyrera, and Raz needle suspensions have been abandoned over the years due to high failure rates. The introduction of a new theory of continence by Petros and Ulmsten in the 1990s, called the integral theory, changed the approach to continence from obstructive to stabilizing the bladder neck and urethra.

The TVT is the first procedure employing a tiny incision and mesh sling placed under no tension, and can be performed as an outpatient under local anesthesia. The procedure does not routinely require catheterization post operatively, and can be routinely performed in under 30 minutes. Continence can be tested during the procedure. It's an outpatient procedure with

discharge in 3-4 hours. There is little pain, and many patients do not even need pain meds. Persistent or chronic pain occurs rarely. A recent systematic review and meta-analysis indicated that persistent or chronic pain occurs in 0.3% of retropubic midurethral sling patients, and 1.2% of trans-obturator midurethral sling patients. (Tommaselli GA, et al., Medium-term and long-term outcomes following placement of midurethral slings for stress urinary incontinence: a systematic review and metaanalysis. Int Urogynecol J 2015 Sep;26(9):1253–68.) Most women can drive a car the next day, resume working within two days, return to normal exercise in just one week. The large pore size allows rapid tissue incorporation and is anchorless, which decreases post-operative pain and voiding dysfunction. Because there are no anchoring sutures or fixation screws, there is no possibility of local bone pain or infection. The design of the covering sheath provides protection to the mesh during deployment and de-tensioning, reducing the risk of infection and distortion of the sling. The technique has a quarter-inch incision in the vagina requiring one suture to close and two exit puncture sites that can be sealed with a Band-Aid.

The success rates for TVT are consistently 80-95% with studies carried out up to 17 years. TVT can be performed safely in women of advanced age, and is the ideal procedure for previously failed incontinence surgeries and even the most severe Type 3 intrinsic sphincteric incontinence. The sling can be deployed either retropubic or transobturator, providing a versatility that expands the indications for use. Either approach avoids an abdominal incision and extensive surgical dissection required by fascial slings and the Burch procedure.

The mesh used in the TVT and TVT-O is a macroporous polypropylene monofilament knitted weave that is soft, elastic, and well-tolerated by the body, which incorporates the material and becomes a permanent support structure that allows fibroblastic and collagen deposition to provide a new neoligament supporting the mid urethra. The polypropylene monofilament has been safely used in surgery as suture throughout the body for over 40 years, and has been shown to be stable and does not degrade in the body over time. TVT and TVT-O implantation is easy to teach and readily learned by both residents and experienced surgeons with reproducibility. Furthermore, the popularity of the devices has led to a greater number of Urologists and Gynecologists offering incontinence treatment to an increasing number of women.

Unlike the Burch or fascial sling, the TVT family of products come with instructions for use, a tracking lot number for safety and batch analysis, as well as MDR reporting and FDA analyses. The devices are not met with cultural or religious objections like allografts or xenografts, and are extremely effective and durable with very low recurrence rates in patients aged 30-80 years. There is a positive net effect on overactive bladder symptoms with improvement in one third to one half of patients after TVT. Additionally, there is a net positive effect on sexual function—no more urinating during intercourse and consistent improvement in validated quality of life questionnaires. A 2012 study with 2-year follow-up that looked at sexual function and activity following midurethral sling placement reported significant improvements in sexual function after both retropubic and transobturator sling procedures. Dyspareunia, incontinence during sex, and fear of incontinence during sex all improved significantly after surgery. (Zyczynski HM, et al., Sexual activity and function in women more than 2 years after midurethral sling placement. Am J Obstet Gynecol 2012 Nov;207(5):421.e1–6.) In fact, one recent systematic review and meta-analysis found that dyspareunia following

implantation of retropubic and transobturator midurethral slings was rare. (Schimpf MO, et al., Sling surgery for stress urinary incontinence in women: a systematic review and metaanalysis. Am J Obstet Gynecol 2014;210:1.e1-1.e27.)

TVT has more RCTs and long-term data than any other incontinence treatment. The TVT and TVT-O are easily studied, patients can be counseled on the vast data, and the study data can be compared to other products and surgical approaches. It is comforting as a surgeon to be using a product that is known to have the largest amount of peer-reviewed data from multiple institutions substantiating a safe, reliable, reproducible technique and material. Prolene has been around for 50 years, been safely used in various applications, and the body's reaction to the material is known. Moreover, surgeons desire polypropylene slings, as over 90% of meshes for SUI are polypropylene. The favored approach is transvaginal, midurethral, and supported by all the specialty societies.

The design optimizes safety by avoiding the large abdominal incision needed for a Burch and fascial sling. A 1.5 cm vaginal incision compared to a 6-8-inch abdominal incision for a Burch or multiple incisions for a fascial sling. The trocars used to pass the sling are tapered with a blunt tip so as to pass through the tissues atraumatically as compared to Stamey needles, which are sharper. Passage of the trocars through the retropubic space has been performed for 50 years, and surgeons are familiar with the anatomy. Complications are usually surgery-related and not mesh-specific. Bladder injury occurs in less than 5% of patients, and occurs as a result of trocar passage, which is managed by re-passage of the trocar and placement of a catheter for 24 hrs. The bladder puncture heals rapidly and completely. Plaintiff's experts may contend that the TVT and TVT-O trocars are passed "blindly" and that that is unsafe. But the use of cystoscopy insures that the TVT trocar passages have not perforated the bladder. Multiple cadaver studies show that with proper technique, trocars are passed with an anatomic margin of safety. The design of the helical passers used with the TVT-O is such that it avoids neurovascular structures. Furthermore, bladder and bowel perforation can occur with the Burch procedure as well. I have directly observed post-Burch bladder perforations of the sutures causing infection, bleeding, and stone formation.

Exposures are uncommon and manageable, occurring in about 1-3% of cases. The cause can be poor tissue integrity caused by estrogen deficiency, delayed wound healing due to diabetes, steroid usage, hematoma formation, or placing the sling too superficially. Treatment includes application of topical estrogen cream, re-closure of the mucosal edges, and limited mesh excision if necessary. The excision can be performed in an office setting under local anesthesia or under light sedation in an OR. Dyspareunia is rare because the TVT's and TVT-O's design positions the mesh placement under the midurethra, via the distal anterior wall incision, at a part of the vaginal wall where the forces and stress from penile contact are minimal. And the design of the TVT provides for the mesh sling to traverse up (vertically) away from the vagina, while the design of the TVT-O provides for the mesh sling to traverse laterally away from the vagina.

Obstructive voiding dysfunction occurs in less than 10% of cases and can be readily managed by either opening the incision in the first few days and loosening the sling or waiting 3-4 weeks to incise the sling under local anesthetic. Continence is preserved 90% of the time. Contrarily, an obstructive Burch procedure will require opening the abdominal incision and

taking down the previous repair which entails a more morbid and protracted recovery with probable recurrent incontinence.

Infection is extremely rare due to the macroporous mesh allowing the immune cells—macrophages—to remove possible bacteria. Fibroblasts and blood vessel incorporation allows for tissue regeneration and incorporation of the mesh into the body. Due to the permanence of the sling, recurrent incontinence is uncommon. The inert nature of polypropylene avoids the risk of rejection and infection, which can occur with allografts and xenografts. Since the material is not biologic, there is no risk of virus or prion transmission.

Single-incision and mini slings—while appropriate, safe, and effective devices under certain circumstances—have less efficacy and far less data to support their use over full-length slings. Multifilament mesh has been previously established to be poorly tolerated by the tissues with an unacceptable infection and encapsulation rate. Larger pore mesh does not have the same support characteristics, and does not have supporting data to prove equivalence with the established Ethicon mesh that has 17-year published follow-up.

As discussed above, laser-cut mesh has no clinical difference when compared to mechanical-cut mesh in the physiologic range of stress when implanted in the female pelvis. (ETH.MESH.01784823-28 (CER Laser Cut Mesh); ETH.MESH.01222075-79 (Elongation Characteristics of Laser Cut Prolene Mesh for TVT); ETH.MESH.06696367-79 (Performance Evaluation of TVT U Prolene Mesh); Lin AT, et al., In Vivo tension Sustained by Fascial Sling in Pubovaginal Sling Surgery for Female Stress Urinary Incontinence, J Urol , 2005 Mar;173(3):894–897.) The only difference is aesthetic, as any particles lost on mechanical-cut mesh cause no harm, as it is the same Prolene used in suspension procedures, Burch or fascial sling fixations.

All surgical procedures have inherent risks. All pelvic surgeries have similar risks, and the introduction of the TVT and TVT-O slings has served to decrease complications when compared to previous techniques. Because native repairs and cystourethropexies do not involve a kit product, complications are not reportable to the MAUDE database. Scientific research has provided improved materials and applications to both improve efficacy and decrease complications. Synthetic mesh that is microporous or too macroporous has proven to be either less safe or less efficacious. If the mesh is too lightweight or too large pore, there is inadequate support.

Ethicon has taken extensive steps to ensure the proper use of its products. The IFU, Surgeon's Monograph, Professional Education training, including didactic lectures and cadaver labs, proctorships, and webinars were designed to offer an extensive resource for the pelvic surgeon to learn the indications for use, surgical technique, and avoidance and management of potential complications. The combination of residency training, previous surgical and clinical experience, and the training resources provided by Ethicon led to many pelvic surgeons gaining expertise in the use of its products, which continues to this day.

All pelvic surgery has similar and inherent risks. Pelvic floor surgeons should be and are aware of the potential complications involved with any surgical treatment of SUI based on a

combination of their medical school education, their residencies, fellowships, their experience, their continuing education, and their review of the device's IFU if a device is used. Risks such as infection, scarring, inflammation, bladder damage, bowel damage, ureter damage, nerve damage, injury to vessels, wound complications (such as wound dehiscence, herniation, hematoma, seroma, pelvic abscess, exposure, and erosion), pain, pelvic pain, groin pain, dyspareunia, fistula, anesthetic risks, bowel or bladder dysfunction, failure of the operation, bleeding, death, pulmonary embolism, myocardial infarction, pneumonia, deep vein thrombosis, and need for reoperation are basic elemental surgical risks of any pelvic floor surgery involving mesh. Surgeons understand that these complications can happen, and they also understand that the symptoms can range in terms of severity and duration.

Surgeons are expected to understand the anatomy in which they are operating, and should identify and dissect in safe planes, avoiding inadvertent damage to the organs and vessels contained within the pelvis. The education and training of the pelvic surgeon should be adequate to know the possibility of complications and their avoidance, risks of recurrence and reoperation. Indeed, the development of biologic and synthetic materials was motivated by the high failure rate of pelvic reconstruction due to the weakness of the patients' connective tissue leading to the condition requiring repair. There is an extensive body of medical knowledge in the medical literature discussing the possibility of complications with the use of meshes. Surgeons' prior experience with mesh informs their understanding of potential complications with pelvic floor surgeries, including those involved with mesh devices. While mesh exposure is unique to mesh devices, it is obvious, and it is general knowledge within female urology and urogynecology. The potential injury to vessels and organs caused by trocars is well-known to surgeons, and potential mesh exposure and foreign body reactions are common knowledge.

Furthermore, the FDA issued a Public Health Notification in 2008 regarding the use of synthetic mesh for treatment of prolapse and incontinence. It alerted healthcare practitioners to "complications associated with transvaginal placement of surgical mesh to treat Pelvic Organ Prolapse (POP) and Stress Urinary Incontinence (SUI)." It noted that the complications were rare, but could have serious consequences, and that the "most frequent complications included erosion through the vaginal epithelium, infection, pain, urinary problems, and recurrence of prolapse and/or incontinence." It also noted that there were "reports of bowel, bladder, and blood vessel perforation during insertion," and that "[i]n some cases, vaginal scarring and mesh erosion led to a significant decrease in patient quality of life due to discomfort and pain, including dyspareunia." This Public Health Notification was yet another source of knowledge for surgeons regarding potential complications associated with synthetic mesh midurethral slings, complementing the TVT and TVT-O's IFU, Ethicon's professional education seminars, and the surgeons' training, education, and experience.

Based upon the analysis above, and on my education, my training, my experience using these products and alternative incontinence treatments, and my reading of the literature referenced above, I believe the TVT and TVT-O slings are not defective, but are reasonably safe for their intended use and have a positive benefit-to-risk profile; better than the Burch and native tissue slings. In my opinion, the benefits of the TVT and TVT-O slings far outweigh the risks of using the devices. The devices are the gold standard and standard of care for treating stress urinary incontinence. At the time the products were launched, I do not believe they could have

been made safer for their intended use. The products were state of the art at the time they were launched, and remain so today.

Date: 2/29/16

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